3.46

James Owens, Esquire
Office of Regional Counsel
U.S. Environmental Protection Agency
Region 1
JFK Federal Building
Boston, MA 02203

Re: Interstate Uniform Services Corp.
EPA Docket No. 83-1006 (Consent Orde

Dear Mr.Owens:

Enclosed for your review is ERT's Ev[illegible] Report prepared pursuant

ERT
A COMSAT COMPANY
ENVIRONMENTAL RESEARCH & TECHNOLOGY, INC.
ATLANTA • CHICAGO • CONCORD, MA • DENVER • FORT COLLINS, CO
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September 24, 1984

BY HAND

James Owens, Esquire
Office of Regional Counsel
U.S. Environmental Protection Agency
Region 1
JFK Federal Building
Boston, MA 02203

Re: Interstate Uniform Services Corp.
EPA Docket No. 83-1006 (Consent Order)

Dear Mr.Owens:

Enclosed for your review is ERT's Evaluation and Recommendation Report prepared pursuant to paragraph six of the above-referenced consent order.

Due to xeroxing difficulties of which I have just been made aware, the first page of the Report is not entirely legible. In the interest of complying with the deadlines under the Order, I am sending this copy notwithstanding. I will provide you with a correctly xeroxed copy of the Report tomorrow.

Sincerely,

Roberta K. Schnoor

RKS:MDc
Enclosure

EVALUATION AND RECOMMENDATIONS FOR ALTERNATIVES CONCERNING ADDITIONAL INVESTIGATION OF GROUND-WATER CONTAMINATION

ERT Document No. P-B961-820

September 24, 1984

Prepared for

UNIFIRST CORPORATION
Woburn, Massachusetts

ENVIRONMENTAL RESEARCH & TECHNOLOGY, INC.
696 Virginia Road, Concord, Massachusetts 01742

TABLE OF CONTENTS

1. INTRODUCTION

1.round

ptember of 1983 a consent order was entered into by the Ur.tes Environmental Protection Agency (EPA) and UniFirst Co (UniFirst) in In the Matter of Interstate Uniform S.Corp., EPA Docket No. 83-1006. Under this order, UniFirst urto perform certain investigatory activities at and near the Uracility at 15 Olympia Avenue, Woburn, Massachusetts (site) tne the potential, if any, for activities at the site to have cd to the introduction of chlorinated solvents to ground whe site area. Environmental Research & Technology, Inc. (ERT) and Goodwin, Proctor & Hoar (GP&H) were retained by UniFirst to pispectively environmental engineering expertise and legal c

onsent order required that two investigations be u. The procedures for these investigations are described in A A and B to the consent order. Appendix A requires a site siessment describing the historical development of the site arst's activities on the site. Appendix B, outlines a study p (the Monitoring Program) to define the potential for the s sources, of tetrachlorethylene contamination at well S-6 to e adient from the site and well S-6. The consent order p or two reports to be submitted to EPA in connection with the a described in Appendix B. The first of these reports must dhe execution and findings of the Monitoring Program. If the M Program shows no findings of tetrachloroethylene c.ions greater than 50 parts per billion (ppb) in any of the m wells, UniFirst is required to submit a second report precommendat...s for further investigation based on the f

1.2 Report Objective

This report has been prepared in accordance with the last-described provision of the consent order, since under the Monitoring Program no tetrachloroethylene was found in any of the seven new wells installed upgradient from the UniFirst building and well S-6. Using data derived from the Appendix A site source assessment, the Monitoring Program, EPA and other studies and information, this report considers the alternatives for additional investigation and recommends what further action, if any, should be undertaken by UniFirst.

2. SUMMARY OF SITE SOURCE ASSESSMENT AND GROUND WATER MONITORING PROGRAM

2.1 Site Source Assessment

The Appendix A report entitled "Assessment of Ground Water Contamination Potential at Interstate Uniform Services Corporation, Woburn, Massachusetts" (the Site Source Assessment), was submitted to EPA in October 1983. The report prepared by ERT describes the development of the site and UniFirst's activities at the site and assesses the possibility that the site is a source of tetrachloroethylene. A summary of the report is provided in this section.

Tetrachloroethylene was in use or in storage at the site for two distinct periods. A small volume, "white shirt" dry cleaning operation was conducted in building B (Figure 1) beginning in 1966 when building B was completed until some time in 1968. Tetrachloroethylene was used as the solvent for the dry cleaning process. The dry cleaning operation was small, so that only five to six 55-gallon drums of tetrachloroethylene were used each year. Tetrachloroethylene was periodically drawn from a tapped 55-gallon drum on an as needed basis. There is no knowledge or record of any spills when dry cleaning was done at the site.

The only waste that resulted from the dry cleaning, other than the wastewater which was discharged to the sanitary sewer, was the diatomaceous earth used for the continuous tetrachloroethylene filter. This waste, known as still bottoms, was a combination of the residuals resulting from the distillation of dirty tetrachloroethylene and the diatomaceous earth filter material. This waste, according to UniFirst officials, contained approximately 20 percent tetrachloroethylene by weight, was non-flowing, and was generated at a rate of approximately five gallons per week.

The waste was disposed of by either drum containerization and transport to a municipal landfill, or placement in a facility dumpster and subsequent disposal by a commercial refuse hauler. UniFirst officials stated that the dumpster as shown in Figure 1 was located on

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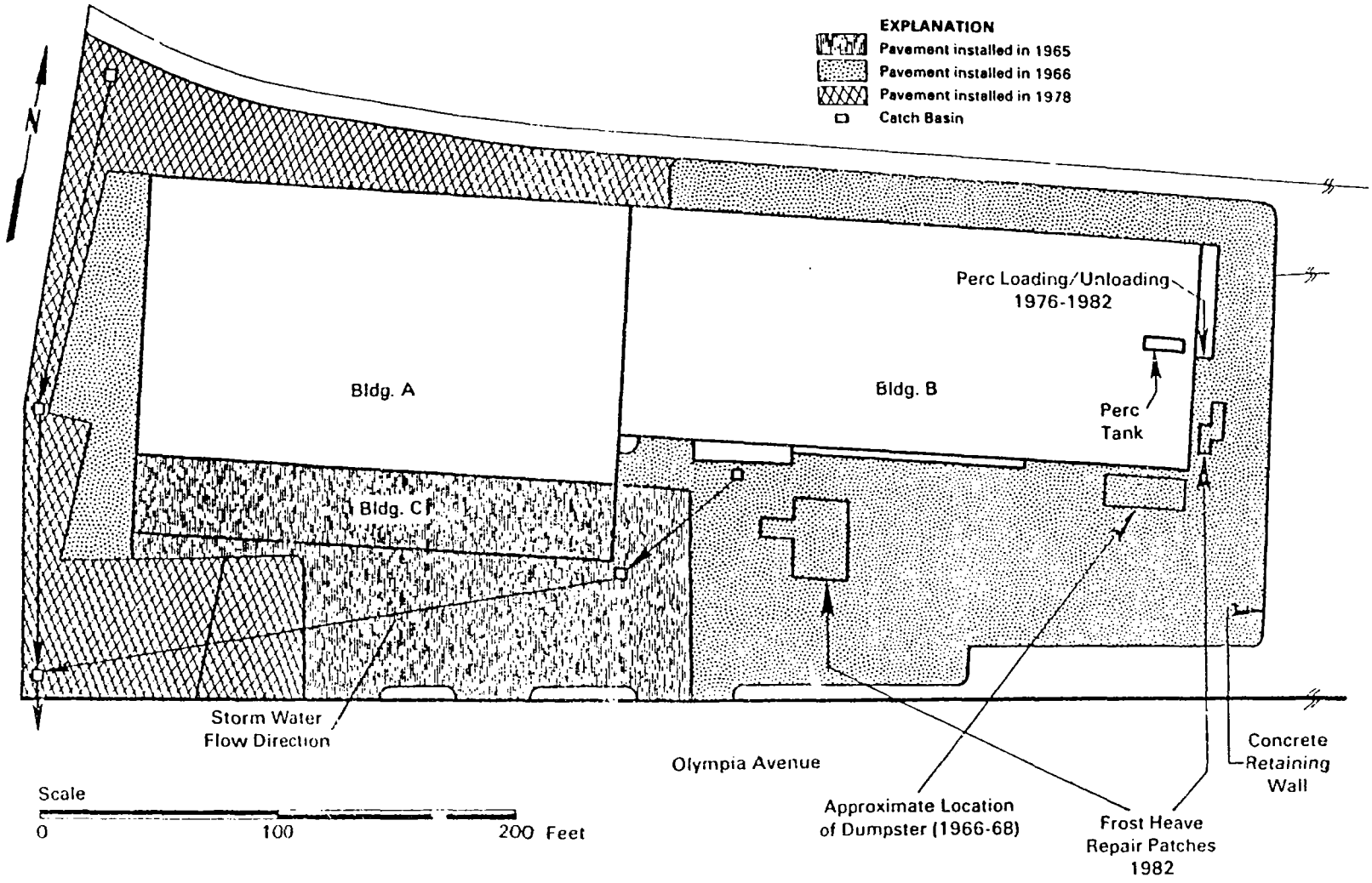

Figure 1 Site Plan and Development History

a paved portion of the site. According to UniFirst officials none of the still bottoms were disposed of on the site or the surrounding property.

The second and only other period when tetrachloroethylene was present on the site was between 1977 and 1982. UniFirst officials have reported that tetrachloroethylene was stored in a 5,000 gallon tank located above ground within the eastern portion of Building B. It was supported on cradles and underlain by a concrete floor. UniFirst officials report that the tank was installed in 1977 and was emptied and removed from the building in November 1982.

UniFirst officials reported that one spill of perc of undetermined size (estimated by UniFirst officials to be less than 100 gallons) did occur within the building in 1979. While pumping perc into the tank, excess perc overflowed a vent which was located on top of the tank in the building. The perc flowed out of this vent, down the sides of the tank onto the concrete floor of the building and pooled there. UniFirst employees stated that no perc flowed out of the building via doors or other passageways, and no floor drains or weep holes were observed, during the site inspection, from which perc spilled on the floor could exit the building. UniFirst employees and officers report that the spill was cleaned up by placing used garments (uniforms, trousers, and shirts) onto the spill, absorbing the perc on the material and carting the garments to another UniFirst owned and operated location which had a dry cleaning operation to extract the perc contained in the garments for reuse.

From 1977 and until its removal in 1982, tetrachloroethylene stored in the tank was transferred to tank trucks which transported it to other UniFirst facilities. These facilities, in turn, supplied the dry cleaning chemical and other laundry products (soaps, hangers, etc.) to route trucks distributing to small retail-level laundries. This type of utilization resulted in infrequent filling of the tank and more frequent draining of smaller quantities to tank trucks at the loading dock of building B. From 1980 until November 1982 when the tank was removed, the tank was used solely for the long-term storage of tetrachloroethlyene in order to take advantage of fluctuations in

tetrachloroethylene wholesale prices. It was reported that all transfer to and from the tank took place at the building B loading dock.

The grading of pavement in the immediate area of the loading dock causes drainage to form a small pool on a low paved area which is estimated to be able to contain 5 to 10 gallons of liquid. Overflow from this small low area and the rest of the surrounding paved area flows in the predominant westerly direction, over pavement in the plant's driveway to Olympia Avenue and then to a municipal storm drain located in Olympia Avenue at the western end of the Site. This storm sewer drains to the Aberjona River. Pavement along this flow path and around the remaining paved area was observed to be sound.

As part of the Site Source Assessment, ERT also attempted to draw some conclusions concerning the ground-water hydrology in the vicinity of the site. On the basis of an integrated potentiometric surface map constructed by Ecology and Environment, Inc., ERT determined that ground water flow in the area of the site and well S-6 is generally in a southwesterly direction. Yet the scale of the map and density of data points on it (the wells) prevented precise definition of the flow paths in the site area. In addition, the interrelationships among varying water transmitting properties of sediments, local irregularities in the bedrock, and vertical gradients had not been established. This not only led to difficulty in determining the upgradient direction from the site and well S-6, but also raised questions as to whether upgradient information would actually be relevant to local ground-water flow.

The Site Source Assessment supports the following conclusions:

- The wastewater generated from the dry cleaning operations drained to wash troughs which routed the wastewater to the municipal sanitary sewer.
- In the event that a solvent spill did occur from dry cleaning operations, the spilled liquid would have drained to the wash trough and also discharged to the municipal sanitary sewer.

- There is no evidence, record or recollection by responsible officers of the company of any spills of tetrachloroethylene outside of the building other than minor drips on the pavement beneath the loading dock outside of building B.
- Any drips would have been of insufficient volume to cause the present levels of contamination found in well S-6.
- Had any larger amounts of tetrachloroethylene been spilled in this area, it is reasonable to believe that the spill would have flowed toward the storm sewers on Olympia Avenue, some portion of it evaporating in the process.
- Any portions of the site that would have received spilled tetrachloroethylene during tank transfers were paved, further reducing the potential for tetrachloroethylene to migrate to the ground water.
- Responsible officers of the firm who have been present at the site during its history and would be aware of any waste disposal operations do not report any spills or other uncontrolled releases on the property outside of the buildings.
- There is no evidence of chemical waste disposal at the site nor is there any evidence which is inconsistent with the recollections, or lack thereof, by company officials.
- Because the only information on ground-water hydrology in the area of the site is preliminary and very general, it is difficult to draw conclusions as to the specific pattern of local ground-water flow.

2.2 Monitoring Program

The Appendix B report entitled "Summary of Monitoring Program UniFirst Corporation, Woburn, Massachusetts", was submitted to EPA in August of 1984. The report, prepared by ERT, was performed to investigate the presence, if any, of tetrachloroethylene in ground water in wells believed to be upgradient from the site and well S-6. The Monitoring Program included a phased approach to the installation of ground-water monitoring wells at three locations. Location UC-1

consists of a single well and Locations UC-2 and UC-3 comprise three-well clusters in which the three wells are placed at different depths in the aquifer. Figure 2 displays the location of these wells and the potentiometric surface elevations at these wells within the area surrounding the site.

The observed water-table elevations indicate that the local potentiometric surface in the unconsolidated deposits overlying bedrock decreases in elevation towards the south and west.

No tetrachloroethylene was detected in the ground-water samples collected from the wells at locations UC-1, 2 and 3.

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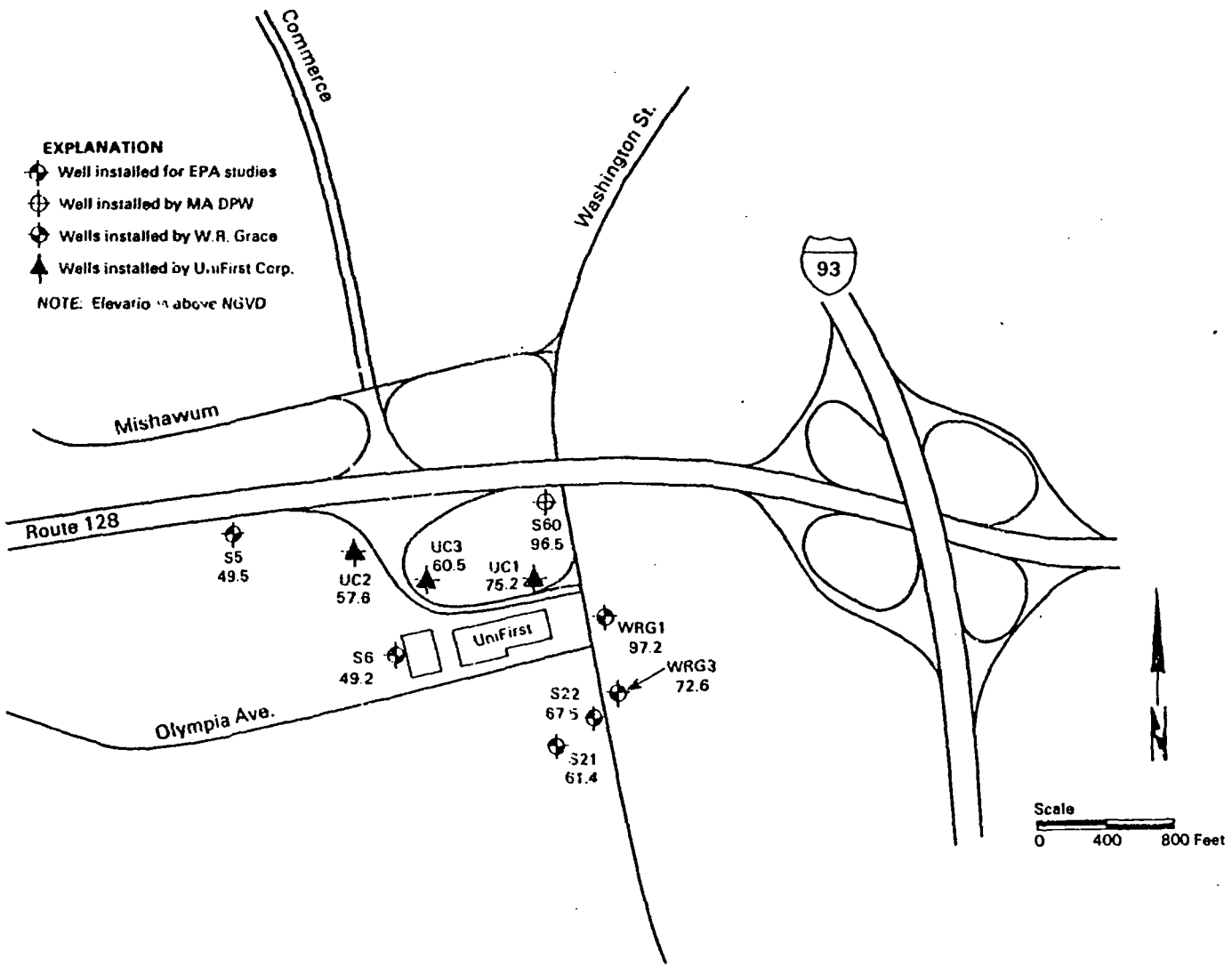

Figure 2 Site Location Map and Potentiometric Surface Elevations as Measured July 18, 1981

3. IMPLICATIONS OF THE SOURCE-LOCATION INVESTIGATION

3.1 On-Site

The Site Source Assessment was undertaken to assess the likelihood a source of tetrachloroethylene contamination existing on-site could be the source of the tetrachloroethylene contamination detected in well S-6. No evidence was found which would indicate that the UniFirst site is a source of tetrachloroethylene contamination to ground water. In fact, the evidence discovered during the assessment suggests that it is not. Moreover, the review of hydrogeologic information, conducted as part of the assessment, revealed no certain relationship between the ground water flowing under the site and well S-6.

3.2 Upgradient from Well S-6 and the Site

The Monitoring Program included installation of ground-water monitoring wells upgradient from well S-6 and the site. The three monitoring locations were constructed to screen a large portion of the saturated thickness within the unconsolidated deposits and the upper bedrock. No tetrachloroethylene was detected in these wells.

Tetrachloroethylene has been detected, however, in ground water at monitoring wells S-21, S-22, WRG-3S and WRG-3D, as shown in Figure 2, as a result of analyses carried out by other parties (Table 1). WRG-3S and WRG-3D (WRG 3 location) represent a shallow and deep monitoring-well cluster located near the southwest corner of the W.R. Grace Cryovac Division property on Washington Street. Wells S-21 and S-22 are located southwest of the WRG-3 location and are screened in the unconsolidated deposits and highly fractured bedrock (Ecology and Environment, 1982). The sites of tetrachloroethylene contamination to the east of UniFirst are also located distinctly upgradient of wells G and H and obliquely upgradient of well S-6.

As Table 1 indicates, WRG-3D, S-21 and S-22 contain varying amounts of tetrachloroethylene, trichloroethylene and trans 1,2 dichloroethylene, all of which substances are also found in well S-6.

TABLE 1

CONCENTRATIONS OF THREE CHLORINATED HYDROCARBONS IN GROUND WATER

WOBURN, MA.

Well Number	Sample Date	Depth Range[1] Screened (feet)	Bedrock Range[1] Screened (feet)	tetrachloro-ethylene	trichloro-ethylene	trans 1,2 dichloroethylene
S-60	04-27-83	34.0-44.1	34.0-44.1	ND	ND	ND
	06-15-83			ND	ND	ND
	11-03-83			ND	ND	ND
UC-1	05-01-84	12.0-26.5	11.7-26.5	ND	ND	ND
UC-2A	05-01-84	71.0-89.0	71.0-89.0	ND	ND	ND
UC-2B	05-01-84	40.0-55.0	N/A	ND	ND	ND
UC-2C	05-01-84	10.0-20.0	N/A	ND	ND	ND
UC-3A	05-01-84	47.0-62.0	55.0-62.0	ND	ND	ND
UC-3B	05-01-84	30.0-45.0	N/A	ND	ND	ND
UC-3C	05-01-84	4.8-24.6	N/A	ND	ND	ND
S-5	11-03-81	4.0-65.5	56.0-66.0	2	ND	ND
S-6	11-03-81	4.0-94.0	84.0-94.0	240	5	10
	04-27-83			220	4	17
	06-15-83			499	79	64
S-22	11-03-81	4.0-44.0	36.5-44.0	4	170	52
S-21	11-03-81	4.0-31.0	21.0-31.0	98	520	420
WRG1-S	06-30-83	-	-	ND	ND	ND
	08-30-83			ND	ND	ND
	11-08-83			ND	ND	ND
WRG1-D	06-30-83	-	-	ND	ND	ND
	08-30-83			ND	ND	ND
	11-08-83			ND	ND	ND
WRG-3S	06-30-83	-	-	17	558	660
	08-30-83			33	785	1230
	11-09-83			29	1160	1800
	11-09-83			34	1180	1940
WRG-3D	06-30-83	-	-	28	908	1010
	08-30-83			62	910	1680
	11-09-83			40	2140	2500
	02-09-84			36	1660	1780
G	07-28-80	-	N/A	43	400	11
	07-28-80			24	140	7
	01-00-81			36	210	14
H	01-00-81		N/A	41	73	21

[1]Footage measurements are below ground surface.
NA - Not applicable.

ERT has no evidence that either trichloroethylene or trans 1, 2 dichloroethylene were ever present on the UniFirst site, and UniFirst officials report that they were not knowingly used, stored or disposed of at the site by UniFirst.

The presence of the same three contaminants in wells S-6, S-21, S-22 and WRG-3D raises more questions than it answers. At a minimum the detection of these contaminants at these three locations presents the possibility that there may be sources of tetrachloroethylene other than the UniFirst site and, further, that these sources may, instead of UniFirst, be the source of the well S-6 contamination. This possibility exists despite the fact that initial indications are that the general direction of ground-water flow in this area is to the south and west. Ground-water transport patterns in fractured bedrock may differ significantly from the pattern of transport in overlying unconsolidated deposits (Caswell, 1984). Particularly with compounds heavier than water, such as tetrachloroethylene, bedrock transport of ground water may cross apparent potentiometric gradients. The presence of known sources of tetrachloroethylene to the east of well S-6, the absence of a known source on the UniFirst property, and the knowledge that the bedrock surface in this area is highly fractured strongly suggest that the source or sources of tetrachloroethylene contamination of well S-6 may be sites other than UniFirst.

3.3 Vicinity of Well S-6

To ERT's knowledge, no one has performed a detailed investigation to determine if the tetrachloroethylene contamination found at well S-6 is occurring as a result of a source nearby well S-6. ERT performed a brief investigation of land-use in this area west of the site which consisted in part of a review of aerial photographs taken in 1938, 1963 and 1968. The 1938 photograph shows the land in the vicinity of well S-6 to be wooded and containing wetlands. A 1963 photograph shows this area as developed for light industry and vegetated. Photographs taken in 1966 and 1972 clearly show a wetland and a drainage swale that conducts stormwater run-off from the north from an asphalt-paved parking area (Charrette Corp.) to the wetland.

This wetland was located to the west of the area where well S-6 now exists. In these photographs there is no indication of waste disposal or other potential sources of tetrachloroethylene.

ERT has also learned from UniFirst, that during the 1970s a rug cleaning business was located in the building directly next to well S-6. According to UniFirst employees who are knowledgeable of rug cleaning, tetrachloroethylene is commonly used as a solvent during rug cleaning operations and therefore tetrachloroethylene may have been present in this building.

Well S-6 is screened from four feet below the ground surface to a total depth of 94 feet. Fill underlies the surface to a depth of two feet. Naturally occurring till underlies the fill to a depth of 84 feet where the bedrock surface was encountered. The construction of well S-6 provides a sampling point which is a gross indicator of ground-water contamination and does not allow for vertical delimitation of ground-water quality. Therefore, it cannot be determined if the tetrachloroethylene is confined within a distinct depth range or, more unlikely, (from ERT's field experience) if the tetrachloroethylene is uniformly distributed throughout the ground-water column intercepted by well S-6. In the course of previous studies, however, it was determined that contaminants are likely to be moving through the bedrock (Ecology and Environment, 1982).

If the contamination could be vertically delimited in well S-6, the distance of a potential source from well S-6 could be approximated. For example, if tetrachloroethylene was known to be confined to the fill, one could assume with a high degree of confidence that the source was located in the immediate vicinity of well S-6. Conversely, if the tetrachloroethylene was known to be confined to the bedrock, the source or sources would most likely lie at substantial distances from well S-6.

At this point, ERT speculates that well S-6 is drawing the tetrachloroethylene contaminated ground water from the upper bedrock. This theory is derived from ERT's monitoring well sampling during the Monitoring Program.

Based on the drawdown characteristics of Wells UC-3A and UC-3B, it is reasonable to believe that in the site area the top of the bedrock is far more permeable than the till. During sampling at the UC-3 well cluster, purging of shallow (UC-3B) and deep wells (UC-3A) was completed using a submersible pump which yielded approximately one gallon per minute. Well UC-3A yielded purge water continuously whereas complete drawdown was achieved at well UC-3B during the same purging conditions. Both of these wells are constructed in the same manner and of the same materials. The difference in yield characteristics is solely attributable to the characteristics of the deposits in which the wells are screened. Each well has a fifteen foot screen though the UC-3A screen extends seven feet into the bedrock and the UC-3B screen is sealed in the till. These conditions indicate that permeabilities are higher in the upper bedrock than in the till. The higher permeability results from flow through bedrock fractures, flow through the weathered and fractured top of the bedrock, or a combination of the two.

Based on the above interpretation, it is reasonable to believe that well S-6 is predominantly recharged during purging from the upper bedrock. Well S-6 is screened in 10 feet of rock and 30 feet of till and yields water continuously during purging. This suggests that either the tetrachloroethylene in well S-6 enters predominantly from the bedrock or it exists in higher concentrations within the saturated portion of the till and becomes diluted during purging by the ground water entering from the bedrock. Hypotheses can be drawn as to the depth range through which contamination is entering well S-6, and the direction from which this contamination migrates into the well. To establish these facts conclusively, however, further investigation in the area of well S-6 would be necessary. This investigation would include a determination of local flow patterns in the bedrock and fill so any vertical delimitation of contamination could be interpreted with respect to source direction.

4. ALTERNATIVES FOR FURTHER INVESTIGATION OF SOURCE LOCATION

4.1 Vicinity of Well S-6

First, the relationship between well S-6 and wells G and H must be investigated. A review would be made of available pumping test information to define the former Aberjona Valley fill aquifer flow conditions during the pumping of wells G and H. If sufficient data does not exist to define the dynamic aquifer conditions created by operation of wells G and H, an actual pumping test would be performed. The purpose of this activity would be to define the potentiometric surface and the cone(s) of influence which existed during pumping of wells G and H so that the aquifer recharge characteristics can be determined and the existence of a relationship between well S-6 and wells G and H either confirmed or denied.

If a relationship between well S-6 and wells G and H is established, further investigation in the vicinity of well S-6 is needed. Section 3.3 discusses the lack of information on where the contamination is entering well S-6. In addition, the probable direction and distance of well S-6 from the source of contamination has not been investigated.

In order to investigate these conditions a series of monitoirng wells clusters would be installed in a pattern that radiates in a general upgradient direction to the north and east from well S-6. During the drilling of the borings for the monitoring wells, samples of soil and rock would be collected and selectively submitted for volatile priority pollutant analyses (EPA-Method 624).

An essential objective of this investigation would be to determine the ground-water flow direction in the upper bedrock. In addition, the investigation would pay particular attention to determining the relationship between the contamination at well S-6 and the contamination encountered at apparently cross-gradient locations WRG-3, S-21 and S-22. Ultimately the new wells installed in the vicinity of well S-6 would provide vertical and horizontal delimitation of the contamination influent to well S-6, determination of the direction in which the contamination flows into well S-6, and sufficient data to isolate the source of contamination.

4.2 On-Site

Further investigation at the site would require a sampling and analysis program of ground water and soil on the site. Ground-water sample analyses would be used to define the presence of contamination. Monitoring wells would be installed to intercept the ground-water so that ground-water samples could be collected from discrete zones within the saturated thickness. Additionally, while drilling the borings for the monitoring wells, samples of soil and bedrock would be collected and selectively submitted for volatile priority pollutant chemical analyses (EPA Method 624).

Monitoring wells would be placed in clusters at or near each corner of the property at the site. The rationale behind the selection of these locations is to bound the site both upgradient and downgradient and establish monitoring points which would allow the characterization of the ground water flowing onto and away from the site. Wells would be placed in clusters of two or three depending upon the depth to bedrock. The number of wells at each cluster would be determined from the thickness of the saturated unconsolidated material overlying bedrock. Each cluster would consist of a deep well with a screen sealed in the top ten to fifteen feet of the bedrock, and one or two additional wells sealed at distinct depths accordingly to intercept ground water from a large portion of the saturated unconsolidated soil. Samples would be obtained of ground water from each of the wells and submitted for volatile priority pollutant chemical analyses (EPA-Method 624).

To support the ground-water and soil analyses a second phase on-site investigation could be performed to characterize the presence, if any, of contamination in the areas of the former tetrachloroethylene storage tank and the waste dumpster. Samples would be taken from cores of soil and construction material such as flooring from beneath the former tetrachloroethylene storage tank. In addition, soil and paving materials at the dumpster location would be similarly sampled. All samples will be analyzed for volatile priority pollutants (EPA-Method 624).

4.3 Upgradient

To further explore the potential that the source of tetrachloroethylene lies upgradient from the site, additional monitoring wells would be installed to provide monitoring points between the existing wells (i.e. WRG-3, WRG-1, UC-1, UC-2, UC-3 etc.). The new wells would be constructed in clusters to establish monitoring points vertically through the saturated unconsolidated deposits and the upper bedrock. Each well cluster would consist of two or three monitoring wells, depending upon the thickness of saturated unconsolidated deposits, with screens sealed at distinctly different elevations and would include one sealed bedrock monitoring well. While drilling the borings for the monitoring wells, samples of soil and bedrock would be collected and selectively submitted for volatile priority pollutant chemical analyses (EPA-Method 624).

The placement of the new wells in combination with the existing wells would effectively create a boundary that would allow for the interception of ground water from the potential upgradient flow directions. The new wells would enhance the likelihood of detecting an pgradient source. It would be essential that this program would include determination of the ground-water flow pattern in the upper bedrock. Furthermore, the installation of bedrock wells would provide additional data to support the assembly of a bedrock surface contour map for the site area. The borings made for the deep monitoring wells would be located in the areas where high bedrock fracturing has been observed (Ecology and Environment, 1982). The overall program would provide information which would be additive to any existing bedrock data and necessary for a site area characterization directed at source identification. Samples of ground water would be obtained from each of the wells, and submitted for volatile priority pollutant chemical analyses (EPA-Method 624).

5. DISCUSSION OF SITE AREA GROUND WATER QUALITY

To evaluate the foregoing alternatives it is necessary to put the nature of the contamination in the vicinity of well S-6 in the appropriate context with respect to its influence on well G and H and the future use of the Aberjona Valley fill aquifer.

The well S-6 is not an actual or potential drinking water source. Its only significance is its hypothesized relationship to wells G and H. ERT believes that a direct connection has not been established between the contamination at wells G and H and the contamination at well S-6.

Even if one were to assume that the tetrachloroethylene contamination in wells G and H results solely from contamination that flows from the well S-6 area, it is not clear that the drinking water from wells G and H has presented a human health hazard. The Woburn Health Study by Lagakos, Wessen and Zelen, which provides the only evidence that the water from wells G and H may present human health concerns, has been sharply criticized by many including reviewers of the study at the Centers for Disease Control (CDC) (see Appendix Stan C. Freni, M.D., Ph.D., MSPH, Renate D. Kimbrough, M.D. and Matthew Zack). Moreover, the levels of tetrachloroethylene that have been found in wells G and H are at or below drinking water standards (see Appendix A Dr. Rudolph Jaeger to Mr. Jeffrey Lawson). Indeed, even the level of tetrachloroethylene detected in well S-6 is much lower than the drinking water standard yielded by a margin of safety risk management approach. This approach to a tetrachloroethylene water standard is the one suggested by a leading toxicologist Dr. John Doull, a member of EPA's Science Advisory Board and past Chairman of the National Academy of Sciences Committee, which developed the risk assessment standards for use in setting contaminant levels under the Safe Drinking Water Act. (see Appendix Dr. Rudolph Jaeger to Science Advisory Board).

Moreover, wells G and H have historically exhibited other types of contamination which have made them unfit as untreated drinking water sources since their installation. The Aberjona Valley fill aquifer in the area of wells G and H has been documented by

investigators, including Whitman & Howard Inc. (1968-1969), Dufresne-Henry (1977) and the Office of the Regional Environmental Engineer (Massachusetts DEQE 1977-1979), to produce water that contains concentrations of manganese that are over an order of magnitude above the drinking-water standard of 0.05 parts per million (ppm). Moreover, sodium concentrations in this aquifer have required the notification of consumers so that people with cardiovascular conditions could account for the elevated sodium levels in their diet. In addition, elevated concentrations of chloride, sulfate, nitrates, hardness and coliform bacteria (for a brief time) have been observed in the ground water withdrawn from this aquifer. These characteristics were noted by the Office of the Regional Environmental Engineer on numerous occasions over the years from 1964-1979 and as the problems persisted, it was ultimately recommended that the water should be treated by sand and granulated activated carbon (GAC) filtration (Dufresne-Henry, 1978, DEQE, 1978). This recommendation was made prior to discovery of chlorinated hydrocarbons in wells G and H. This history indicates that wells G and H are unsuitable as untreated drinking water sources irrespective of the tetrachloroethylene contamination found in them.

6. CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

Based upon the work performed by ERT and all referenced data and information, the following conclusions can be drawn:

- Studies performed to date show that the potential is very low that the UniFirst site is source of tetrachloroethylene contamination in groundwater.
- Sound conclusions as to the relationship between any unknown contamination at the site and well S-6 cannot be drawn.
- The contamination found at well S-6 appears to originate in bedrock, which suggests that the site is not the source due to its proximity to well S-6, the likelihood that well S-6 is recharged from ground water contained in the bedrock, and the history of general asphalt pavement and limited use of tetrachoroethylene at the site.
- Tetrachoroethylene has been detected cross-gradient from the site and well S-6, at the WRG-3 location and at wells S-21 and S-22 indicating that other sources of the tetrachloroethylene contamination may exist in addition to or instead of UniFirst.
- These wells also exhibit other contaminants that are found in well S-6 and are not known to have been used at the UniFirst site.
- There is an obvious lack of information regarding bedrock flow in the site area and in the area of wells G and H. Bedrock flow would have to be defined in order to ascertain whether a relationship exists between tetrachloroethylene contamination of wells G and H and the contamination of wells S-6, S-21, S-22, WRG-3D and any other contamination from the site.
- The ground water contained in the Aberjona Valley fill aquifer, has, since the installation of wells G and H, required treatment prior to use as a potable water source

because of contamination by a variety of substances other than tetrachloroethylene.

- The tetrachloroethylene level in well S-6 is well below the safe drinking water level established by use of a risk management strategy that some toxicologists recommend should be used for tetrachloroethylene.
- The tetrachloroethylene levels in wells G and H are at or below safe levels established under even more conservative risk management assumptions.
- The conclusions of the Woburn Health Study by Lagakos, Wessen and Zelen, which purports to establish a relationship between the contamination of wells G and H and deleterious health effects, has been called into question by criticisms from a number of reviewers from CDC.

6.2 Recommendations

Although the work done under the consent order focused on determining the source of the tetrachloroethylene contamination of wells S-6, well S-6 is not drinking water source. An important question that has not yet been answered is whether there is a relationship between ground water contamination at well S-6 and wells G and H. Further study would be required to determine this. Only if it is established that contamination at S-6 is linked to contamination at wells G and H, does the question of the source of the well S-6 contamination become at all relevant.

The work that has been performed by UniFirst under the consent order does not reveal the source of the S-6 contamination. On the contrary, it indicates that there is a very low potential that the UniFirst site is the source of the S-6 contamination. In view of these findings, several alternatives could be pursued to determine whether other sources of the contamination exist. The work done by ERT suggests that, if a connection between well S-6 and wells G and H were sufficiently established, one or more of the following might be considered: a site source assessment of the area in the vicinity of well S-6; the undertaking of resampling and analyses at well S-6; a

program to establish the relationship between S-6 and WRG-3, S-21 and S-22 which would likely include the installation of monitoring wells and ground-water sample analyses.

With more studies, it is possible that the source of the contamination of well S-6 could be located. The expense associated with a program of this magnitude, however, would be very large, and it is uncertain that clear cut answers would be obtained.

The ultimate concern of both EPA and UniFirst is the contamination in wells G and H. As is noted elsewhere in this report, the level of tetrachloroethylene in those wells is already at or below safe drinking water levels, and, recent comments on the Woburn Health Study indicate that a connection between wells G and H and adverse human health effects has not been established.

Prior to the detection of tetrachloroethylene contamination, MA-DEQE suggested that wells G and H be treated with sand and GAC filtration to remove other contaminants then known to be present in the water. A combination of sand and GAC filtration would remove not only naturally occurring contaminants, but would reduce the concentrations of chlorinated hydrocarbons as well (EPA, 1980, Calgon Corp., 1983). To install such treatment would be much more cost-effective than pursuing additional expensive field investigation.

Accordingly, ERT recommends that no further investigation be undertaken by UniFirst at this time.

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APPENDIX

September 17, 1984

Mr. Jeffrey Lawson
Environmental Research & Technology, Inc.
696 Virginia Road
Concord, MA 01742

Re: Safe Water Levels for Tetrachloroethylene

Dear Mr. Lawson:

You have asked me to clarify the relationship between the levels of tetrachloroethylene found in certain wells in Woburn, Massachusetts and the comments submitted by Dr. Nathan Karch and myself to the Science Advisory Board of EPA ("SAB") as well as the comments submitted to the SAB by its member toxicologists Drs. John Doull and Marvin Kuschner, all of which documents you have reviewed. This letter responds to your request.

As I understand the Woburn data, a June 1983 test of an EPA monitoring well designated S-6 revealed a tetrachloroethylene level of 499 parts per billion ("ppb"). In addition, tests performed at Wells G and H, which in the past have been used by the City of Woburn for drinking water and are located at some distance from well S-6, detected levels of tetrachloroethylene in those wells of up to 43 ppb.

I believe that two observations about risk management and the levels of tetrachloroethylene found in the Woburn wells are appropriate. First, under the risk management approach recommended in the collection of toxicological comments you have in your possession, even the levels of tetrachloroethylene found in well S-6, which is not a drinking water source, would be at or below accepted safe drinking water standards. Second, even if a very conservative multistage model risk assessment were employed, the levels of tetrachloroethylene found in wells G and H would be at or below the drinking water standard produced by that model.

After reviewing EPA's Draft Health Assessment Document for Tetrachloroethylene and the public comments and testimony on it,

Drs. Doull and Kuschner of the SAB submitted written comments expressing disatisfaction with treating tetrachloroethylene as a non-threshold human carcinogen in view of the inadequacy of the evidence to support this conclusion. The inconclusive nature of the evidence on tetrachloroethylene is accurately reflected in the International Agency for Research on Cancer ("IARC") classification of tetrachloroethylene as a Group 3 substance which means, in IARC terminology, that tetrachloroethylene "cannot be classified as to its human carcinogenicity." Dr. Doull proposes that IARC's judgement should be reflected in the risk management approach adopted for tetrachloroethylene and other Group 3 substances. He suggests that "[i]t may be useful, for example, to consider the Safe Drinking Water Committee approach for Category 3 agents (ADI with safety factor)" and to reserve risk assessment for substances that can with confidence be classified as carcinogens. The approach favored by Dr. Doull is elaborated upon in the letter of May 7, 1984 from Dr. Karch and myself to the SAB, which on pages 8 and 9, sets out the margin of safety approach to setting a standard for tetrachloroethylene. Although my calculations in that letter are intended to establish an ambient air standard for tetrachloroethylene, a drinking water level can be derived from the same data.

As you will note, the calculations in our letter are based upon the preliminary data from the recent National Toxicology Program ("NTP") bioassay which suggests that no statistically significant increase in tumors occurred in a gavage study performed on female B6C3F1 mice at a dose of 25 mg of tetrachloroethylene/kg body weight/day administered in corn oil. Assuming that a mouse dose can be converted into an equivalent human dose, this "dose" translates into a human drinking water consumption level of 875 ppm. This is based on a conversion of the 25 mg tetrachloroethylene/kg body weight/day dose to a total dose based on a human body weight of 70 kg (25 mg tetrachloroethylene kg body weight/day X 70 kg body weight = 1750 mg tetrachloroethylene/day). This "dose", 1750 mg tetrachloroethylene per day, is equivalent to the no observed effect level ("NOEL") in the mouse. Assuming an average daily drinking water intake of 2 liters, the NOEL can be expressed as 875 ppm (1750 mg tetrachloroethylene/day divided by 2 liters = 875 mg/l = 875 ppm). As this is a dose for which no chronic effects are shown, it can be considered the basis for the acceptable daily intake (ADI) dose sought by Dr. Doull.

To determine the ADI, a safety factor must be applied to the NOEL. The safety factor of 100 is one which has historically been used and is widely deemed acceptable. Yet if one were to consider this factor to be inadequate, the safety factor could be increased by a factor of 10 to 1000. As noted in the May 7, 1984 letter, a safety factor of 1000 is applied to studies in which the data are judged to be inadequate because: (1) a small number of animals were tested or examined; (2) the laboratory practices were suspect; or (3) the data is not yet replicated by other laboratories. If the NTP data for some reason were deemed inadequate, a very conservative safety factor of 1000 could be applied to yield an ADI for tetrachloroethylene of 875 ppb.

The ADI of 875 ppb, derived through the scientifically accepted method of applying a margin of safety to a NOEL, is twice as high as the level of tetrachloroethylene which has been observed in well S-6. Moreover, it should be stressed that well S-6 is not used as a drinking water source but is employed for monitoring purposes only. Thus to measure its quality by drinking water standards is very conservative. The highest level of tetrachloroethylene found in wells G and H is an order of magnitude lower than the levels in S-6 and one twenty-fourth of the 875 ppb level calculated through the margin of safety approach.

To follow up my second point about the relationship between non-threshold risk assessment and the Woburn data, Dr. Kenneth Crump recently performed some computer modeling from which Dr. Karch and I have developed some estimates for a tetrachloroethylene water standard. Computer modeling, based upon the assumption that a non-threshold relationship between dose and carcinogenicity exists, is the risk management approach currently favored by the Cancer Assessment Group ("CAG") of EPA. In particular, CAG frequently relies upon a model known as a multistage model. Dr. Crump ran this multistage model using the recent NTP data. Based upon a virtually safe dose at an upper bound risk level of 1 in 100,000, Dr. Karch and I determined that the multistage model yields a water standard of 42 ppb. Thus even when very conservative assumptions are employed, the drinking water levels of tetrachloroethylene

observed in the past in Woburn wells G and H appear within scientifically established safe levels.

I hope that this explanation fully answers your questions.

Sincerely,

Rudolph J. Jaeger, Ph.D.
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StonyBrook

June 6, 1984

Mr. Ernst Linde
Executive Secretary
Environmental Health Committee
Science Advisory Board
United States Environmental Protection Agency
Washington, D.C. 20460

Dear Mr. Linde:

This is in relation to trichloroethylene and tetrachloroethylene.

The evidence for carcinogenicity is based on the increase in mouse liver tumors.

I remain uncertain and unconvinced of the significance of the increase in liver tumors in the mouse particularly of the $B_6C_3F_1$ variety in which there is a significant background incidence. Further, these increases are obtained at dose levels which are cytotoxic and thus accompanied by regenerative proliferation, a phenomenon which may itself encourage tumor induction in a susceptible strain.

This, together with the absence of good evidence for meaningful "genotoxicity," strongly suggest promotion as the mechanism of tumor induction. This role is consonant with what has generally been thought of as the r le of halogenated hydrocarbons as a group in producing liver tumors.

This possibility affects the interpretation of risk and hazard for it is generally agreed the promotion is a threshhold phenomenon and that it is a reversible effect. I think it entirely reasonable to consider the action of these hepatotoxins as "partial chemical hepatectomy."

In order to assist us in interpreting the data in the case of trichloroethylene and tetrachloroethylene, I would suggest that we ask for an opinion from Dr. Henry Pitot, Director of the McArdle Institute, who has investigated and thought hard about hepatic carcinogenesis and about the possible roles of halogenated hydrocarbons.

I am in agreement with the stated reservations in these documents. I am not entirely persuaded of the sense of doing risk assessments even when

they are qualified by the statement that these assessments would hold if the substances were carcinogens.

I would like to see the promised additional column in the potency table that will give a qualitative evaluation.

Sincerely,

Marvin Kuschner, M.D.
Dean, School of Medicine

MK:es

THE UNIVERSITY OF KANSAS

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39th and Rainbow Blvd., Kansas City, Kansas 66103
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June 6, 1984

To: Science Advisory Board

A review of the health assessment documents for tri- and tetra-chlorethylene and the revisions proposed in the Federal Register, the statements of the Natural Resources Defense Council, the Halogenated Solvents Industry Alliance, and the papers of Elcome and others identify several issues related to the safety of these agents.

1. There is no epidemiologic evidence that tri- or tetra-chlorethylene is carcinogenic in humans.

2. Tri- and tetra-chlorethylene are not mutagenic in conventional test systems. The marginal results obtained with tri-chlorethylene may have been due to added epoxide stabilizers.

3. The oral administration of these and other chlorinated hydrocarbon solvents has been shown to induce hepatocellular carcinoma in B6C3F1 mice but not in other species.

4. The kinetics of biotransformation of halogenated hydrocarbon solvents is markedly species-dependent. With trichlorethylene, for example, the Vmax/Km (TRI to TCA) for mice is 10 times more sensitive than in the rat and 100 times more sensitive than in human hepatocytes. Further metabolic saturation occurs in the rat and other species but not in B6C3F1 mice.

The IARC criteria for limited evidence of carcinogenicity includes: a) positive results in a single species, strain or experiment, b) the use of inadequate dosage levels or exposure duration, too few animals and poor survival, follow-up or reporting, and c) studies where the neoplasms occur spontaneously and are difficult to classify as malignant histologically (lung and liver tumors in mice). The revised statement on the carcinogenicity of these agents places them in Category 3 of the IARC classification (limited evidence), and this classification is consistent with previous decisions of the SAB and the NAS Safe Drinking Water Committee. I agree with this classification for both trichlorethylene and tetrachlorethylene.

The decision of CAG to utilize the IARC classification system for carcinogenicity has been supported and encouraged by the SAB on several

previous occasions, and when combined with the weight of evidence described in Dr. Paynter's Standard Evaluation Procedure document, represents a logical and scientifically defendable course of action for the agency. It seems to me that the main issue here is not whether there should be sub-categories in the IARC Category 3 (with Tri and Tetra in the high 3 category) but rather whether there should be different risk extrapolation methods for Category 3 agents. It may be useful, for example, to consider the Safe Drinking Water Committee approach for Category 3 agents (ADI with safety factor) and to reserve the Weibull extrapolation method for Category 1 and 2 agents. This is an area that needs to be considered by the SAB in conjunction with the various agency groups utilizing these approaches.

Rudolph J. Jaeger, Ph.D.
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(201) 945-5927 (evenings)

May 7, 1984

Science Advisory Board
c/o Mr. Ernst Linde
Scientist Administrator
Science Advisory Board (A-101)
Environmental Protection Agency
301 M Street, SW
Washington, DC 20460

Dear Sirs:

The following letter is submitted to the EPA in the matter of my review and comments on the Draft Health Assessment document of Tetrachloroethylene (Perchloroethylene). It is the basis for my presentation to you on Wednesday, May 9, 1984. The letter is addressed to the Project Officer for Tetrachloroethylene.

Sincerely,

Rudolph J. Jaeger, Ph.D.
Diplomate, American Board of Toxicology
Consulting Toxicologist
Research Professor, New York University Medical Center

encl.

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403 Nelson Avenue
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May 7, 1984

Dr. Mark Greenberg
Project Officer for Tetrachloroethylene
Environmental Criteria & Assessment Office (MD-52)
U.S. Environmental Protection Agency
Research Triangle Park, North Carolina 27711

Dear Sir:

As I advised in my letter of March 3, 1983, I am writing to provide you with additional comments on the external review draft of the Health Assessment Document for Tetrachloroethylene. Although this submission is beyond the date set for receipt of comments to the EPA, it is my hope that you will consider these views in your revision of the draft document on Tetrachloroethylene (perchloroethylene). This letter will be the basis for a presentation on May 9, 1984 to the Science Advisory Board, who we hope will consider these views in their overall evaluation of the draft document.

As I indicated to Dr. Goldstein in my March 3, 1984 letter, I have been retained by the law firm of Goodwin, Proctor & Hoar, of Boston, Massachusetts in connection with litigation in the State of Vermont, as well as administrative proceedings soon to be commenced there to set ambient standards for toxic air contaminants. In generating these comments, I have sought the assistance and collaboration of Doctors Nathan Karch and Robert Golden of Karch & Associates. Dr. Marvin Schneiderman, a former Associate Director for Field Studies and Statistics of the National Cancer Institute and a consultant to Karch & Associates also participated in the preparation of these comments. Because of a potential conflict of interest through his participation on a national committee to which Dr. Schneiderman has very recently been appointed, Dr. Schneiderman is no longer involved with me on this project. Dr. Schneiderman's participation ended on April 30, 1984.

We have examined the carcinogenicity risk assessment provided in chapter 9 of the draft Health Assessment Document in greater detail, and the revision of chapter 9 (contained in Dr. Goldstein's letter), and we wish to make a number of comments about the assumptions upon which the assessment is based and the techniques used in performing the assessment.

To begin with, Chapter 9 states that its purpose "is to provide an evaluation of the likelihood that tetrachloroethylene (perchloroethylene) is a human carcinogen and, on the assumption that it is a human carcinogen, to provide a basis for estimating its public health impact, including a potency evaluation, in relation to other carcinogens." Based only on the 1977 NCI bioassay in male and female B6C3F1 mice and an indirect reference to a recent NTP bioassay in female B6C3F1 mice, the chapter now concludes equivocally that tetrachloroethylene (perchloroethylene) is "close to a probable human carcinogen," while recognizing that a substantial body of scientific opinion regards such mouse data as suspect. Using only the data from the 1977 NCI bioassay, the section includes a remarkable estimate that tetrachloroethylene (perchloroethylene) is more potent than vinyl chloride and benzene (potency index of 6 x 10 to the zero power for tetrachloroethylene (perchloroethylene) versus 1 x 10 to the zero power and 4 x 10 to the zero power, for vinyl chloride and benzene, respectively).

Whatever may be the incentives to treat tetrachloroethylene (perchloroethylene) as if it were a human carcinogen (and we do not think them sufficient), Chapter 9's "close to a probable human carcinogen" conclusion and associated risk estimate are not warranted either by the data or by the authorities on which they rely. Rather, the question is: "How likely is it that tetrachloroethylene (perchloroethylene) is a human carcinogen?" If one must make a reasoned judgement based only on the existing data, a more scientifically defensible conclusion is that, as a strictly scientific matter, the data are inconclusive. As a result, they simply do not justify the quantitative risk assessment presented.

The first assumption in performing the risk assessment was that tetrachloroethylene (perchloroethylene) is a carcinogen in the mouse and is, therefore, a presumptive human carcinogen. As I indicated in my letter of March 3, 1984, I believe that the evidence from long-term bioassays as well as the biochemical studies that are or soon will be available in the literature do not establish tetrachloroethylene (perchloroethylene) as an animal carcinogen in other strains and species. In addition, there reportedly are a number of bioassays that are soon to be released under the auspices of the the National Toxicology Program (NTP) and at least two European laboratories. Although these studies are not yet completed and published, they may raise more questions than they answer about the potential carcinogenicity of tetrachloroethylene (perchloroethylene).

With regard to the current NTP bioassay program, we understand that there is an inhalation bioassay of tetrachloroethylene (perchloroethylene) which is currently in progress. Our understanding of the status of the gavage bioassay in mice and rats, recently completed by the NTP, is that the mouse data are in draft form and under internal review. The preliminary data from this study reportedly establish

tetrachloroethylene (perchloroethylene) as a carcinogen in the B6C3F1 mouse. Orally administered doses equal to or greater than 50 mg tetrachloroethylene (perchloroethylene)/kg body weight/day showed statistically significant increases in tumor incidence but the lowest dose tested, 25 mg tetrachloroethylene (perchloroethylene)/kg body weight/day, did not.

This dose may or may not reflect the true no-effect level if larger populations are tested. In this study and at this group size, this dose was the no-effect level. The preliminary data in rats are not as far along in the analysis, but there appears, at this time, to be no evidence of carcinogenicity of tetrachloroethylene (perchloroethylene) in the rat. Based on these reports, this study might be regarded as a second, or confirming study for the carcinogenicity of tetrachloroethylene (perchloroethylene) in the mouse.

Two research groups in Europe have conducted studies in which different strains of mice were used, and these studies reportedly fail to show evidence of carcinogenicity. If true, this suggests that the apparent observed carcinogenicity in the B6C3F1 mouse is strain-specific.

The suggestion from preliminary information about the European bioassays, even if taken alone, might raise serious doubt about the applicability of the mouse findings in the NCI or the NTP study to humans. Additional biochemical studies investigating the ability of tetrachloroethylene (perchloroethylene) and trichloroethylene to induce peroxisome proliferation are also available in preliminary form. These reports have been made available to me as a personal communication by Dr. C. Elcombe of Imperial Chemical Industries and his associates. These data suggest that peroxisome proliferation, and the subsequent alteration in fat metabolism and generation of hydrogen peroxide, may be specific to the mouse (and absent or considerably reduced in the rat), and perhaps specific to the B6C3F1 strain of mouse. Further data that point to the absence of peroxisome proliferation by human liver tissue in vitro and in vivo may be forthcoming from studies of therapeutically administered hypolipidemic agents. These agents are known to be associated with peroxisome proliferation in animals.

Taken as a whole, then, I believe that even if tetrachloroethylene (perchloroethylene) is shown to be carcinogenic in the B6C3F1 strain of mouse, there is considerable doubt that it poses risk to humans as a carcinogen because it may act through a different mechanism in the B6C3F1 mouse than in rats or humans. Many questions, of course, need to be addressed in the ongoing studies. These include, among others, whether it can be demonstrated by biochemical investigation that the increased hydrogen peroxide produced in the B6C3F1 mouse as a consequence of peroxisome proliferation overwhelms the ability of catalase and other enzymes to destroy the hydrogen peroxide which

is produced by this secondary pathway of fat metabolism. Another question is whether peroxisome proliferation, which may be specific to the B6C3F1 strain of mouse, is a dose-dependent phenomenon. That is, it occurs only when other metabolic pathways are saturated.

If it is a dose-dependent phenomenon, the application to human risk assessment of the B6C3F1 bioassay data derived from high doses would be appropriate only under conditions where high human exposures exist. Lastly, the B6C3F1 mouse appears to be an exceptionally responsive animal to some agents. Because of unknown causes, whether of a biochemical or pathophysiologic origin, it appears to have a predisposition to tumor development. Thus, results obtained in this rodent may be bear minimal relationship to the human population for selected toxicants. Its utility in other circumstances must be judged separately.

A coherent picture of the mechanism of action of tetrachloroethylene (perchloroethylene) liver toxicity thus seems to be emerging. Perchloroethylene may induce peroxisome proliferation in the B6C3F1 mouse liver but to a lesser extent or not at all in the rat or in humans. This picture is inconsistent with the approach taken in the risk assessment described in the draft Health Assessment Document. It is also inconsistent with the judgements made by the International Agency for Research on Cancer (IARC) which EPA references in chapter 9 and with the Third Report on Carcinogens prepared by the Department of Health and Human Services (DHHS).

With respect with IARC, the latest revision to the draft (as amended by Dr. Goldstein's letter) states that according to "a literal interpretation" of IARC criteria, the animal data supporting the carcinogenicity of tetrachloroethylene might be classified as limited" and that "its overall IARC ranking might be classified as Group 3, meaning, according to IARC language, that tetrachloroethylene cannot be classified as to its human carcinogenicity." The amending letter then goes on to state, however:

"It should be recognized that Group 3 covers a broad range of evidence: From inadequate to almost sufficient animal data. Because of the strength of the mouse liver cancer response, tetrachloroethylene is at the upper end of this range. Hence, the classification of the carcinogenicity of tetrachloroethylene under the IARC criteria for animal evidence could be limited or almost sufficient, depending on the nature of the bioassay evidence as it exists today and on the differing current scientific views about the induction of liver tumors in mice by chlorinated organic compounds. Therefore, the overall IARC ranking of tetrachloroethylene is Group 3, but close to Group 2B, i.e. the more conservative scientific view would regard tetrachloroethylene as being close to a probable human carcinogen, but there is considerable scientific sentiment for regarding tetrachloroethylene as an agent that cannot be

classified as to its carcinogenicity for humans."

The language in the preceding quotation is based on an interpretation of the "strength" or potency of tetrachloroethylene (perchloroethylene) from the NCI bioassay among female B6C3F1 mice. The same response was seen at both the high and low dose. In contrast, the preliminary NTP bioassay in female B6C3F1 mice appears to demonstrate a dose-response relationship which would imply a very different potency than that inferred by EPA from the NCI data. Furthermore, the language in the above quotation seems to imply that IARC's criteria do not accommodate the boundary problem posed by tetrachloroethylene (perchloroethylene). IARC states flatly that "tetrachloroethylene is carcinogenic to mice, producing malignant liver neoplasms", and yet IARC still classified the animal data as "limited." This position seems not to depend upon the "strength" of the mouse response. Rather, it seems to follow from IARC's explicit judgement that animal data should be classified as "limited" where "the neoplasms produced often occur spontaneously and, in the past, have been difficult to classify as malignant by histological criteria alone (e.g, lung and liver tumours in mice)."

Similarly, the Department of Health & Human Services is charged by P. L. 95-622 to publish an annual report which contains "a list of all substances (i) which either are known to be carcinogens or which may reasonably be anticipated to be carcinogens and (ii) to which a significant number of persons residing in the United States are exposed." Perchloroethylene is not listed in any of the Department of Health and Human Services annual reports, including the most recent Third Annual Report on Carcinogens issued in 1983.

Accordingly, EPA should treat tetrachloroethylene (perchloroethylene) as a non-carcinogenic substance (we should note that this is a finding which, as far as any substance is concerned, could change as additional substantive information appears). Such treatment would not necessarily decide the question of what risk management approach to use. For example, one might apply a safety factor to the observed no-effect level for hepatic or renal toxicity. Such an approach was used by the National Academy of Science in 1980 when the Academy developed a seven-day value for the Significant No Adverse Response Level (SNARL) of 24.5 mg tetrachloroethylene (perchloroethylene)/liter in drinking water. This value contained a 100 fold margin of safety. A value for a chronic SNARL was not developed because of the lack of availability of a no-effect level.

Philadelphia and the State of New York have employed an approach based on defined margins of safety in setting guidelines for ambient air limits for tetrachloroethylene (perchloroethylene). Based on a review conducted by a multidisciplinary panel of advisors, Philadelphia set an annual standard of 1200 ppb for tetrachloroethylene (perchloroethylene)

which they computed by dividing the TLV (50,000 ppb) by 42. New York chose to divide the TLV by 300 and set an annual standard of 166 ppb for tetrachloroethylene (perchloroethylene).

If tetrachloroethylene (perchloroethylene) were considered a carcinogen in the mouse on the basis of the NTP bioassay, at a minimum EPA should use the dose-response data from that bioassay in preparing the final document. Though in preliminary form, the NTP mouse data seem to exhibit a dose response relationship, in contrast to the data from the NCI bioassay in which the same response was observed at the high and the low doses.

Given the differences between the two bioassays, in any case, the use of the NCI bioassay in the draft document for risk extrapolation is indefensible. As I indicated in my letter, I have had conversations with the principal authors of the NCI bioassay protocols who agree with this view. The NTP study in mice includes four dose levels and treated (vehicle) as well as untreated controls, although only one sex (females) is included. The preliminary, unreleased data (employed by the National Academy of Sciences in an unreleased and subsequently withdrawn document on drinking water) appear to show a dose related increase in tumors, which is statistically significant in the three highest dose levels but not at the lowest dose. Moreover, as noted above, this finding of carcinogenicity may be a reflection of the biochemistry and/or physiology of the mouse and may not be relevant to human beings.

It is reasonable to assert in the absence of specific clinical data that the experimental data in the NCI study for the female are on the portion of the dose-response curve that no longer exhibits a dose-response relationship because of compound related hepatotoxicity. Further, the data in males is opposite in response to that seen in females even though the administered doses were larger. Thus, the data from the females that was used risk estimation are not monotonic, an assumption necessary for the use of the multi-stage model.

In checking the calculation of the responses predicted from the application of the multistage model to the NCI data, we found that the predicted response at the high dose was considerably higher than the observed response. Similarly, the predicted response at the low dose was considerably lower than the observed response. This suggests a serious lack of fit. The statistical tests for "goodness of fit" also point to the inappropriateness of the NCI data for risk estimation. This test is not a demanding one; yet, the "goodness of fit" shows a marginal lack of fit with two degrees of freedom (p = approximately 0.1). Because the multistage model constrains the dose-response coefficients to take only positive values, some statisticians believe that the degrees of freedom should be reduced. Of note, therefore, is the significant lack of fit when the degrees of freedom are reduced to one (p = approximately 0.03). Thus, the statistical tests tend to confirm our impression of the

inappropriateness of the NCI data for use in this and, possibly any other, risk estimation.

Moreover, in the draft document, while the GLOBAL 79 program is cited, the tabular data suggest that EPA used the WEIBULL 82 program for deriving the unit risk. This program is not a true Weibull model as such, but is a multistage model to which time has been added to dose as an independent variable. In making the extrapolation to low dose with WEIBULL 82, EPA made the assumption that animals that died before the development of the first tumors at 41 weeks should be excluded. Thus, the response at the high dose is changed from 19/48 to 19/45. There is some question about this type of adjustment. We believe such a data adjustment is not defensible. Indeed, even with these corrections of the data to improve the fit, the conformity of the "adjusted" model is not much better than the fit for the simple multi-stage model.

The results for the probit and Weibull models do not fit the NCI data for another reason as well. For all doses calculated in Table 9-5 (page 9-36), the risk is one. This implies that all animals exposed would be expected to develop cancer at each of the projected human doses. This is a situation that has never occurred in humans or animals from any agent of which we are aware.

The data from the NCI bioassay, thus, lead to an artificially high unit risk, which is even more untenable given the considerable questions about whether tetrachloroethylene (perchloroethylene) poses any risk of cancer to humans. We believe that the draft's assertion that the unit risk is consistent with the epidemiologic data is misleading. The data from the NCI animal study were subject to such considerable uncertainties that the confidence intervals calculated on the unit risk are extremely large. Almost any result in the epidemiologic studies would be consistent with these animal data. Thus, such large confidence intervals do not provide a meaningful basis for comparisons between human and animal studies.

Consequently, we believe that tetrachloroethylene (perchloroethylene) is not established as a carcinogen. If an air standard were to be set, a margin of safety approach, a procedure with wide acceptance and use in the field of public health, would appear to be a more appropriate approach to risk management than quantitative risk estimation. Accordingly, a safety factor of 10 would be applied to the NOEL to extrapolate between species (from mouse to man) and a further safety factor of 10 could be used to take into account variations among individuals in the exposed human population. The resulting safety factor of 100, when applied to the apparent NOEL in the NTP study, would lead to a standard of 1.25 ppm (1250 ppb) or so for tetrachloroethylene (perchloroethylene) in air. The basis for this estimate is given below. This value is nearly the same number established by the city of Philadelphia (1.2 ppm). The

Multidisciplinary Health Advisory Panel in Philadelphia applied a safety factor of 42 to the tetrachloroethylene (perchloroethylene) TLV of 50 ppm for an 8-hour work day to yield the resulting value of 1.2 ppm.

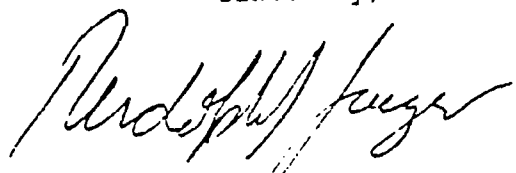
The recommended standard for tetrachloroethylene (perchloroethylene) in air is based on the following calculation. The draft health assessment document states that the NOEL is a level at which no statistically significant increase in effect occurs. The preliminary data from the NTP bioassay suggests that no statistically significant increase in tumors occurred in the gavage study at a dose of 25 mg tetrachloroethylene (perchloroethylene)/kg body weight/day when given in corn oil. With the assumption that 25 mg tetrachloroethylene (perchloroethylene)/kg body weight/day in the mouse can be translated to an equivalent human dose, this "dose" translates to a human air exposure of about 125 ppm during a 24 hour period. This is based on the conversion of the 25 mg tetrachloroethylene (perchloroethylene)/kg body weight/day dose to a total dose based on a human body weight of 70 kg body weight (25 mg tetrachloroethylene (perchloroethylene)/kg body weight/day x 70 kg body weight = 1750 mg tetrachloroethylene (perchloroethylene)/day). This "dose", 1750 mg tetrachloroethylene (perchloroethylene) per day, is equivalent to the no-effect dose in the mouse. This dose is likely to be divided over a total inhaled air volume of 20 cubic meters or so per day (more or less depending on the level of activity but this value has been used by the EPA) so that the exposure concentration may be, on average, 87.5 mg tetrachloroethylene (perchloroethylene) per cubic meter. This can be converted to parts of tetrachloroethylene (perchloroethylene) per million of air by the using factor of 1 ppm being equal to 6.78 mg tetrachloroethylene (perchloroethylene) per cubic meter. Thus, 87.5 mg tetrachloroethylene (perchloroethylene) per cubic meter is equivalent to about 12.5 ppm (depending on assumptions). Since not all inhaled tetrachloroethylene (perchloroethylene) is absorbed and a large fraction is exhaled (excreted) with the expired air (either with each breath or after a delay), it is reasonable to increase this value by a factor of 10, and the resulting value is as much as 125 ppm. As was stated, this assumes that 90% of the inhaled tetrachloroethylene (perchloroethylene) is exhaled unchanged. There may be some variance in this estimate and it may be lower. This concentration is the human equivalent of the lowest administered dose in the NTP study. This value of 125 ppm is the value to which we applied a 100 fold safety margin to arrive at the value of 1.25 ppm tetrachloroethylene (perchloroethylene) in air.

If one were to consider the safety factor of 100 as inadequate, an additional safety factor of 10 could be applied to yield a total safety factor of 1000. This safety factor of 1000 is applied to studies in which the data are judged to be inadequate because a small number of animals were tested or examined, because the laboratory practices were suspect (i.e.,

there was a lack of compliance with Good Laboratory Practice or there were deficiencies in an audit of the data), or because the data was not yet replicated by other laboratories. If the NTP study were judged to be inadequate, the value derived from applying the safety factor of 1000 to the derived value of 125 ppm is 125 ppb. This number is comparable in magnitude and somewhat lower than the value derived by the State of New York in establishing its annual air standard for tetrachloroethylene (perchloroethylene) (166 ppb) by applying a safety factor of 300 to the TLV.

We should note that we do not use this calculation as a "risk assessment." It is, rather, a choice of an approach to "risk management." When all the bioassay and other studies that are currently underway are published, it will be possible to determine with greater accuracy whether there is, in fact, a real and substantial risk of human cancer from tetrachloroethylene (perchloroethylene), by ingestion or inhalation of both. At that time, the EPA could evaluate all of the data from the various bioassays and perform a more scientifically based risk assessment.

Sincerely,



Rudolph J. Jaeger, Ph.D.
Diplomate, American Board of Toxicology
Consulting Toxicologist
Research Professor, Institute of Environmental Medicine
New York University Medical Center

DEPARTMENT OF HEALTH & HUMAN SERVICES

Olga

Public Health Service
Centers for Disease Control

Memorandum

April 23, 1984

From Stan C. Freni, M.D. Ph.D., MSPH
EIS-officer, SSB, CDD, CEH

Subject Review of Report on Woburn Health Study, 1984

To Paul Wiesner, M.D., Director CDD, CEH

Through: Henry Falk, M.D., Chief, SSB, CDD, CEH

As you requested, I have reviewed "The Woburn Health Study", a report from S.W. Lagakos, B.J. Wessen and M. Zelen, statisticians from the Department of Biostatistics, Harvard School of Public Health, February 7, 1984.

SUMMARY

The study was designed and conducted by statisticians, but was presented as an epidemiologic study. Unfortunately, the dominating statistical viewpoint resulted in negligence of epidemiologic issues. The authors concentrated on a statistical association of two contaminated city wells G and H with health effects, but failed to show that the remaining city wells were free of the G and H contaminants. Supposedly unexposed individuals could, therefore, have actually been exposed. Even in the presence of unknown pollutants, specific to G and H wells, the observed statistical association with health effects is subject to doubt as to its validity and accuracy. Errors in the estimation of GH exposure can indeed affect the magnitude and the p-value of the risk estimate, contrary to what the authors have claimed. Further, the authors stated that the association of exposure with health effects could not have been due to chance alone, because 6 out of 18 tests were significantly positive. However, health outcomes have been grouped in a few arbitrary and non-random categories, which is likely to influence the distribution of the p-values. By stating that the conclusion of a positive association of exposure with health effects is valid because of its statistical significance, the authors seriously violated epidemiologic principles. The authors did not provide evidence of temporal sequence of exposure and effect, latency period, biological plausibility, internal consistency, and sufficient control of confounding and recall bias. Lastly, the authors failed to show how contaminated groundwater could induce health effects, while all citizens were connected to the city tapwater system. In conclusion, due to overly emphasizing statistics at the cost of epidemiologic values, the reviewed report failed in providing evidence for a positive and causal relationship between contaminated water and a large number of health effects.

INTRODUCTION

In 1979, pollution of 2 city wells (G and H) was detected, and concommitently a cluster of childhood leukemia was observed in Woburn, Massachusetts. Subsequently, 61 tests wells were found to be tainted. A study of the Massachusetts Department of Health and CDC did not reveal a causal relationship between contamination and leukemia. Because of continuing public concern, statisticians of the Harvard School of Public Health, Department of Biostatistics, decided to assist a citizens' action group by designing and conducting an investigation into the relationship between water contamination, and health effects.

MATERIALS AND METHODS

The study was implemented as a cross-sectional health survey. Exposure was defined as either the availability of water from G and H wells (GH-water) or as living in the Pine Street (PS) or the Sweetwater Brook (SB) areas that had a cluster of tainted test wells. In both cases, exposure was assumed to exist since 1960. The contamination involved chlorinated hydrocarbons, toluene, benzene, lead and arsenic. However, no information was given as to the specific distribution of the chemicals over the wells and on the concentrations. Information on health effects as of 1960 was obtained via a health questionnaire administered by telephone interview of households. One adult per household was asked to respond for all members of the household. All households of Woburn were eligible if at least one member was born in Woburn after 1920. Senior residents and residents arriving in Woburn after 1979 were exluded from the study.

The exposure status of individuals as to GH-water was calculated as an exposure score based on time of residence and the availability of GH-water. The latter was estimated from the results of a study from the Massachusetts Department of Environmental Quality and Engineering, who used a simulation model of the city water distribution system. These results were estimates of the availability (not the use) of GH-water to entire zones rather than to individual households.

RESULTS

The questionnaire survey took 13 months. The eligible population with a listed telephone consisted of 5,880 households of which 1,149 refused to participate. Usable data were obtained from 3,257 households (55%). Of 25 leukemia cases, 15 were eligible, all occurring after 1969. A statistically significant association was found with the availability of GH-water. No correlation was found with abortion or low birthweights. Perinatal mortality was found increased in the PS-area. As to birth defects, no association of exposure with musculoskeletal and cardiovascular abnormalities was found. The association of exposure to GH-water with eye/ear abnormities was significant. A significant association was also found for GH-water in only the PS-area with "environmental" birth defects (a group consisting of neural tube defects, oral clefts, and chromosomal aberrations). There was no relation between exposure and 45 "other" birth defects.

GH-water and the PS-area were associated with childhood disorders (chronic bronchitis, asthma, pneumonia), while GH-water was a risk factor for childhood kidney/urinary problems. Neurologic/sensory disorders in children (epilepsy, convulsions, vision and hearing problems) were associated with living in the SB-area, not with PS area or GH-water.

GH-water and the PS-area were associated with childhood disorders (chronic bronchitis, asthma, pneumonia), while GH water was a risk factor for childhood kidney/urinary problems. Neurologic/sensory disorders in children (epilepsy, convulsions, vision and hearing problems) were associated with living in the SB-area, not with the PS-area or GH-water.

DISCUSSION

Comments on methodology and interpretations are limited to essential points only, to keep this review readable and limited in size.

1. The 55% participation rate is likely to affect the validity of the study outcomes, as all leukemia cases did respond. No effort was made to reveal the reasons for refusal, and the characteristics of the 20% of the eligible population who were excluded from analysis for reasons other than refusal.

2. Exposure originated from estimates of GH-water availability to entire zones, not to individuals. Estimating individual exposure is, therefore, likely subject to large errors.

3. The exposure addresses GH-water availability, not GH-water intake and particularly not the actual intake of any contaminants. The cumulative exposure is, therefore, subject to large errors with regard to the association between toxic compounds and health effects.

4. As 61 test wells were contaminated, it appears very likely that city wells other than G and H were tainted as well. The authors did not give proof to the contrary. Supposedly unexposed people may, therefore, have actually been exposed. Analogously, people living in areas other than PS and SB may have had higher concentrations or more chemicals in the underlying aquifer.

5. The authors defined living above a contaminated aquifer as being exposed, without explaining how groundwater could rise beyond the capillary layer through a thick layer of bedrock to the surface. However, even if such an event could happen, the question remains, how the ingestion or inhalation of the extremely minute amounts of soil tainted with volatiles could result in statistically detectable adverse health outcomes.

6. Exposure scores were based on time of residence since 1960, but exposure could not have started before 1963 when the GH-wells came to production. The association of exposure with diseases prior to 1960, therefore, makes no sense. Moreover, any health effect caused by contaminants at the extremely low doses, typically found in the environment, requires a certain latency period. The temporal sequence of exposure and effect has been ignored. For example, the exposure corresponding with birth defects was estimated in the year of birth, not in the year of conception or in the months of pregnancy.

7. No effort was made to provide evidence that the actual contamination with toxic chemicals started prior to 1979. The kind of pollution prior to 1979 that was discussed is not specific to GH-wells, and concentrations were not mentioned. Virtually all city tapwater in the USA contain chemicals such as iron, manganese, sulfates, etc.

8. The potential errors in the exposure estimate have been said not to affect the risk estimate and its P-value because of randomness. However, this is an invalid statement, because the topographical distribution of cases is not random. Leukemia cases clustered in time and space. It is likely that clustering of other health effects has occurred as well.

9. The expected frequency of diseases other than leukemia was derived from a logistic regression model, based on survey results. However, the authors should have known that the predictive value of any multivariate model (linear, discriminant, logistic) is extremely dubious. It is reflective of the authors' prejudiced approach that they did not use the city, county, state or national data bases of low birthweight, perinatal mortality, and birth defects. Although the reliability of such databases is known not to be great, their consistency over time renders their value at least higher than that of the predictions from a logistic model. The low value of such predictions is illustrated by the strange finding that there was no association between perinatal mortality with maternal age, SES, prior abortion, and parity.

10. The conclusions of the authors, as worded in the text, do not necessarily accord with the data in the tables. For instance, it is not clear how there could be a significant excess perinatal mortality, if table 7.8 shows that there was no excess at all for GH exposure up to a score of 0.6 and for living in the SB-area, while living in the PS-area seemed even to be protective.

11. The authors claimed that when 6 tests out of 18 show statistical significance, the probability that chance alone could explain this result is extremely unlikely. Apparently, the authors support the controversial Bonferroni principle, that addresses the distribution of p-values in the absence of a true association. However, this is a purely statistical issue and does not bear on epidemiologic inferences. Moreover, Bonferroni's principle is based on randomness and the mutual independency of the tests. In this study randomness is unlikely to be present, since the authors divided arbitrarily the large number of diseases studied into a few non-random categories. Apparently, these groups were formed after the data were collected and analyzed, not a priori. This leaves the possibility that the categories have been chosen to fit a desired study outcome.

12. Childhood disorders are reported and accepted for analysis on face value, without verification through medical records, despite the wide publicity of the Woburn case. The authors justified this dubious approach by arguing that the results proved to be consistent with exposure. However, the selective excess of neurologic/sensory disorders in the PS-area, and contrastingly the significant deficit in the SB-area is just one of a number of ignored inconsistencies.

13. Whether or not knowingly, the authors discussed only positive statistical associations. Nowhere in the text did the authors pay attention to negative associations. The reviewer has no means to judge whether or not a negative association (protective effect), hidden in the tables, is significant.

14. This review is not exhaustive. I suffice with a closing comment that characterizes the entire report. The authors stated on page 97 that <u>because</u> a p-value is valid, the association is necessarily valid as well. This violate every concept of epidemiology. The validity of an association between exposure and effect is based on epidemiologic issues, <u>not</u> on p-values. Issues such as temporal sequence, biologic plausibility and latency period have been totally ignored. Control of confounders and the check on internal consistency were insufficient. And, worst of all, the contamination status of non-GH wells, and the exposure status of individuals living in other areas than PS and SB have not been ascertained. This renders the study to become a bad example of an ecologic study rather than the intended cross-sectional study.

14. In conclusion, this report is characterized by overestimation of the value of statistics and ignorance of epidemiologic issues. The authors demonstrate a substantial dose of prejudice, favoring a positive association of exposure with adverse health effects.

Rudolph J. Jaeger, Ph.D.

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March 3, 1984

Project Officer for Tetrachloroethylene
Environmental Criteria & Assessment Office
(MD-52)
U.S. Environmental Protection Agency
Research Triangle Park
North Carolina 27711

Dear Madam or Sir:

I have been retained by the law firm of Goodwin, Procter & Hoar, Boston, Massachusetts in connection with litigation in the State of Vermont, as well as administrative proceedings soon to be commenced there to set ambient standards for toxic air contaminants. I have been asked to consult on the toxicologic evaluations and risks associated with occupational and environmental exposure to tetrachloroethylene (referred to as perchloroethylene). My qualifications are appended to this letter as Appendix 1.

In addition to my own expertise, I have sought the collaboration of Karch & Associates (Dr. Nathan Karch and Dr. Robert Golden who are being assisted by Dr. Marvin Schneiderman) of Washington, D.C. These individuals have substantial expertise in the area of biostatistics, quantitative risk assessment and hazard evaluation. Their qualifications are enumerated in Appendix 2.

During January of 1984, the United States Environmental Protection Agency (EPA), Office of Health and Environmental Assessment, made its draft Health Assessment Document for Tetrachloroethylene (Perchloroethylene) available for public comment. The requested date for comments by public and other interested parties is March 5, 1984. This date is sufficiently close to the actual release date and general availability of the final, printed version of the review draft as to make extensive comment difficult within the requested time frame. I therefore have chosen to write this

abbreviated letter noting some relevant areas of concern for which my colleagues and I are currently preparing a more complete analysis for use in Vermont. We hope to be able to forward this analysis to EPA later this spring.

I generally am pleased with the document, and I congratulate its authors on the excellent review of the literature that it contains. I am unsettled, however, by the carcinogenicity risk assessment and must note my reasons for concern even if only in outline form for now.

Under the conditions known now to exist in the environment, my assessment of perchloroethylene is based on the material being only marginally risk-producing in the human environment. That is, my focus is that perchloroethylene is a material for which a large body of evidence exists showing it to be potentially hepatotoxic, nephrotoxic and capable of producing central nervous system depression at concentrations above a hundred parts per million for significant fractions of a human or animal life span (for hepatic and renal injury to occur, the amount of time required to produce an effect will depend heavily on the exposure concentration). Even the more sensitive tests which may detect slight central nervous alterations show effects that occur at early exposure time periods and which appear to be reversible. Certainly, none of the literature surveyed by myself or by the EPA suggests a cumulative toxic effect that appears in the absence of gross organ damage, i.e., injury to the liver or kidneys.

When the literature cited by the EPA as well as the concluding sections are examined closely, the observation is repeatedly made that insufficient data exist to conclude that perchloroethylene poses a serious health risk such as cancer in man. According to this literature, the material is a common article of commerce and exposure of large numbers of persons occurs during chemical solvent cleaning of clothing. In addition, exposures to substantial fractions of the threshold limit value occur in the lives of workers in the dry-cleaning industry. Nevertheless, the epidemiology studies are unable to show a clear association of perchloroethylene with a single chronic disease state. Furthermore, several studies are used to support suspicion of concern and to provide a basis for a comparison to animal-based risk assessment. Yet, as noted by the International Agency for Research on Cancer (IARC) and the EPA, these studies are inadequate to demonstrate a causal link to cancer.

When the rodent bioassay is examined, it is found that the data suggest that the material is of low to negligible carcinogenic potential with no concrete proof that a direct carcinogenic risk exists in rodents other than mice. It is well known that mice

are overly sensitive models for hepatocarcinogenesis and may be responding to a promoting effect or repeated injury having been previously initiated by unknown viral or genetic factors. This fact, coupled with the general lack of genetic activity of perchloroethylene, points to the minimal risk posed by the substance.

The bioassay on which the animal-based risk assessment is founded was designed by Drs. John and Elizabeth Weisberger. Both have stated that the use of their one and two dose carcinogenesis bioassays for the purpose of risk assessment is wholly unfounded. This position was reiterated by Dr. Elizabeth Weisberger as recently as last week at the Toxicology Forum which met in Washington, D.C.

The corrected conclusion recently issued by the EPA is now consistent with the position of the IARC, namely, that "there is inadequate evidence for classifying PERCHLOROETHYLENE as a human carcinogen." I am increasingly of the view that the evidence which has continued to accumulate since the IARC monograph on perchloroethylene supports an even stronger conclusion, namely, that perchloroethylene presently appears not to be a human carcinogen. When the negative mutagenicity evidence and the negative non-mouse animal data are taken together with the long history of relatively high occupational exposure, the failure of the epidemiological data to show clear, site-specific signs of carcinogenic activity suggests that the conclusion responsibly to be drawn is that if the substance were a human carcinogen, in all likelihood it would have manifested itself clearly by now.

Accordingly, you can appreciate my concern that the continued inclusion of the carcinogenicity potency and unit risk estimates in the EPA document is both inappropriate and unduly alarming. In particular, the document suggests that perchloroethylene has a potency equivalent to vinyl chloride, a material for which both animal and human evidence show a clear and unequivocal relationship to carcinogenesis. The animal bioassay-based potency analysis, moreover, is unable to detect differences between perchloroethylene and acrylonitrile, an even more potent animal carcinogen for which clear evidence of carcinogenicity exists in two species. In my opinion and from the weight of evidence and the sheer weight of effort expended to date, no such conclusions should be drawn at this time for perchloroethylene.

The estimated upper confidence limit on the unit risk for perchloroethylene in air cited by the document is 1×10^{-2} per ppm exposure concentration. This value is incredible considering the occupational threshold value, 50 ppm, to which many workers have been exposed as a life-time working concentration. The safe

use of this material for so many years and the inability of the sciences of toxicology and epidemiology to show a substantial risk for man makes the present dose-related risk estimate disappointingly large, and its continued promulgation seems to be ill-advised. For materials not known or shown to be carcinogenic, the use of risk estimates that suggest such an outcome leads to a false attribution where fear of exposure and personal as well as economic disruption may produce more real harm than the risk supposedly avoided.

We expect to continue our assessment of this material and, as noted above, to make our fuller analysis available to EPA when it is completed. Please do not hesitate to contact me if you have questions or comments.

Sincerely,

Rudolph J. Jaeger, Ph.D.
Diplomate, American Board of
Toxicology
Consulting Toxicologist

RJ:pah
Encs.

Karch & Associates (202) 723-4155
Consultants in Toxicology, Epidemiology and Risk Assessment

STATEMENT OF CAPABILITIES

Karch & Associates, specialists in toxicology, epidemiology, and risk assessment, has broad-based expertise in evaluating the health and environmental effects of chemical and physical agents. As consultants to a wide variety of clients, including chemical and other manufacturing corporations, law firms, public interest groups, and government, Karch & Associates perform the following kinds of analyses:

- chemistry reviews -- the chemical substances and mixtures to which an individual or population may be exposed.
- hazard evaluations -- the potential for toxicity, including the types of health and environmental effects, the severity of each effect, and the dose-response relationships.
- exposure assessments -- the route, frequency, duration, level and other conditions of exposure and any special susceptibilities or characteristics of the exposed population.
- risk assessments -- estimation of the probability that a particular hazard will be realized in an exposed individual or population.

Services and Applications

These analyses have included litigation support to plaintiffs and defendants, expert testimony, hazard warning and labeling programs, industrial hygiene programs, assessment of potential health and environmental effects of new or existing products, assistance in meeting various regulatory requirements, and policy evaluations for government.

7713 Fourteenth Street, N.W. Washington, D. C. 20012

Examples of the chemical and physical agents with which Karch & Associates and its employees have had direct experience are:

- polychlorinated biphenyls and dibenzofurans
- pesticides, such as heptachlor/chlordane, carbamates, and organo-phosphates
- organic solvents, such as benzene, toluene, and xylene
- volatile organic compounds, such as chloroform, carbon tetrachloride, methylene chloride, and other halomethanes, trichloroethylene, tetrachloroethylene, and other halogenated organic solvents
- 2,4,5-T, trichlorophenol, and other substances contaminated with tetrachlorodibenzodioxin (TCDD)
- vinyl chloride, polyvinyl chloride, and many other polymeric substances
- plasticizers, such as phthalates and adipates, and plasticizer feedstocks, such as phthalic anhydride
- ozone, particulates and other prevalent air pollutants
- petroleum, coal derivatives, and synthetic fuels
- diethylstilbestrol and other synthetic estrogens
- formaldehyde
- asbestos, fiberglass, vermiculite, wollastonite, and other fibrous and particulate materials

Terms of Business

In general, the terms of business for Karch & Associates are on the basis of time and materials, including all reasonable and necessary expenses. However, variations may occur depending upon the nature of the task to be performed. For each task, a written proposal is prepared, which includes a description of deliverables, a schedule for completion, and an estimate of the cost. Actual costs will not exceed the estimate unless authorized by the client. To assure that all client information will remain confidential, security procedures have been implemented. Additional procedures have been instituted to ensure that conflicts of interests will not occur.

Senior Scientists

Nathan J. Karch, Ph.D. Dr. Karch is President of Karch & Associates. He holds a doctorate from Yale University in chemistry, and he has had post-graduate training in toxicology, epidemiology, and biostatistics. As a senior science advisor at Clement Associates, Dr. Karch performed a range of risk assessments on air pollutants, on contaminants of drinking water, on chemicals leaching from hazardous waste sites, and on chemicals posing reproductive hazards. He taught toxicology at Howard University and recently co-authored a book on chemical hazards to human reproduction. As senior staff member for toxic substances and environmental health at the President's Council on Environmental Quality, Dr. Karch worked on various national policies for regulating carcinogens. He also supervised interagency efforts to coordinate research on the assessment of health and environmental risks. As a senior staff officer at the National Academy of Sciences/National Research Council, he worked with committees on a variety of health and environmental issues including the use of scientific and engineering information at the U.S. Environmental Protection Agency (EPA), procedures for regulating pesticides at EPA, and polychlorinated biphenyls in the environment.

Robert J. Golden, Ph.D. Dr. Golden is a Senior Associate at Karch & Associates. He holds a doctorate in environmental toxicology from the University of Michigan. Since 1975, Dr. Golden has served as staff officer, senior staff officer, and project director of the Safe Drinking Water Committee at the National Academy of Sciences/National Research Council. In this capacity, he reviewed and evaluated a wide range of chemical, physical, and microbiological contaminants of drinking water, which were published as a five volume series on Drinking Water and Health. In addition, he worked with committees on carcinogenicity and other health hazards of pesticides, on the health and environmental hazards of aliphatic and aromatic amines, and on quality criteria by which treated wastewater may be reused for drinking.

Karch & Associates has a number of associate scientists located at academic and other research institutions, who contribute to various tasks as the need arises. The expertise of these associate scientists encompasses the following areas: carcinogenesis, inhalation-, developmental-, behavioral-, and neuro-toxicology, pathology of the central nervous system, epidemiology, and biostatistics.

NATHAN J. KARCH, Ph.D.
President, Karch & Associates
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Dr. Karch recently established a new consulting firm in the areas of toxicology, epidemiology, and risk assessment. Recent projects include assistance to private clients in evaluating worker risks and industrial hygiene practices, in reviewing the toxicity of various industrial chemicals and mineral products, and in evaluating scientific issues raised in product liability and related litigation. He also has recently served as a member of the Toxicity Validation Team in the Office of Toxic Substances at EPA and worked on the chemicals that are candidates for significant new use rules (SNURs). For another private client, Dr. Karch prepared an annotated bibliography designed to provide a basis for establishing a library of data on toxic substances.

As a Senior Science Advisor with Clement Associates, Dr. Karch was involved in projects concerned with determining the health and environmental effects of chemicals. For example, he coordinated the preparation of a comprehensive review of chemical hazards to human reproduction for the Council on Environmental Quality (CEQ). For the U.S. Environmental Protection Agency (EPA), he evaluated the health effects of various pesticides and reviewed and evaluated the evidence for cancer and other chronic hazards associated with air pollution For private clients, he prepared an assessment of the role of air pollution as a cause of lung cancer, and he prepared an assessment of the risks of cancer, reproductive impairment, and neurological damage should leaks develop in a proposed crude oil pipeline. He also analyzed the health effects of the chemicals disposed of at a major dump site. He directed an assessment of research on the effects of oil and gas exploration on the ecosystem of the Flower Garden Banks coral reefs in the Gulf of Mexico.

At CEQ, Dr. Karch was Acting Senior Staff Member for Toxic Substances and Environmental Health. In this position he provided scientific support to the Toxic Substances Strategy Committee. For the committee's report to the President on toxic substances, he prepared the sections on cancer and carcinogens, public health and environmental problems, and environmental health research. He also served as a member of the Toxic Substances Control Act Interagency Testing Committee.

As part of a study of EPA's use of scientific and technical information conducted by the National Academy of Sciences, Dr. Karch reviewed and evaluated all of EPA's research and regulatory programs, the sources of scientific and technical information on which the programs relied, and the criteria used for evaluating information under the programs.

EDUCATION

Nondegree courses in toxicology, epidemiology, and biostatistics; the Foundation for Advanced Education in the Sciences (Graduate School at NIH), 1976-1981

Ph.D., Physical Organic Chemistry, Yale University, 1973

M.Phil., Chemistry, Yale University, 1969

B.S., Chemistry, Illinois Institute of Technology, 1966

EMPLOYMENT HISTORY

1982-present	President, Karch & Associates
1980-1982	Senior Science Advisor, Science Director; Clement Associates
1982	Assistant Professor, Toxicology and Epidemiology, Howard University
1977-1980	Acting Senior Staff Member for Toxic Substances and Environmental Health, Council on Environmental Quality (CEQ)
1975-1977	Staff Officer,Senior Staff Officer; National Academy of Sciences/National Research Council
1972-1975	Assistant for Legislative Research, American Chemical Society
1966	Research Chemist, G.D. Searle and Co.
1964-1966	NSF Research Participant, Illinois Institute of Technology

PROFESSIONAL EXPERIENCE

At Clement, supervised contracts and conducted technical evaluations for government and private clients; performed assessments of hazards, exposure, and risks of a wide range of chemical and physical agents, including pesticides, drugs, air and water pollutants, workplace hazards, cosmetic ingredients, and consumer products.

At CEQ, provided scientific staff support for 22-agency Toxic Substances Strategy Committee and prepared committee report to the President; responsible for sections of report on cancer and carcinogens, environmental health research, and public health and environmental problems, each of which concerned risk extrapolation and statistical evaluation of data on health effects.

CEQ Member, Toxic Substances Control Act Interagency Testing Committee; Project Officer for technical support and technical workshop contracts.

CEQ Staff Epidemiologist; supervised consultant conducting epidemiological studies; investigated trends in and conditions of environmental and workplace pollutants and cancer that cause birth defects through use of the integrated data bases in UPGRADE.

Staff Officer, Panel on Scientific and Technical Considerations, Committee on Environmental Decision Making, National Academy of Sciences/National Research Council (NAS/NRC); evaluated EPA's programs, the sources of information on which the programs relied, and the scientific criteria used.

Senior Staff Officer, Pesticide Information Review and Evaluation Committee of the NAS/NRC Assembly of Life Sciences, Board on Toxicology and Environmental Health Hazards.

Senior Staff Officer, NAS/NRC Committee for an Assessment of Polychlorinated Biphenyls in the Environment and Committee for Prototype Explicit Analyses for Pesticides.

MEMBERSHIP IN SOCIETIES

American Association for the Advancement of Science
American Chemical Society
American Public Health Association
New York Academy of Sciences
Society for Occupational and Environmental Health
Society for Risk Analysis

PUBLICATIONS

Nisbet, I.C.T. and Karch, N.J. 1983. Chemical Hazards to Human Reproduction. Noyes Data Corporation, New Jersey. ISBN 0-8155-0931-6; originally published in limited quantity by the Council on Environmental Quality, U.S. Government Printing Office (1981).

Nisbet, I.C.T., Karch, N.J., Schneiderman, M.A., and Siegel, D. 1982. Review and evaluation of the evidence for cancer associated with air pollution. Draft revised report submitted to the U.S. Environmental Protection Agency by Clement Associates under Contract No. 68-02- 3396, December 15, 1982.

Nisbet, I.C.T., Karch, N.J., and Plautz, J. 1982. Effects of drilling muds on the Flower Garden Banks coral reefs. Phase II Draft Report to Anadarko Production Co., Natural Resources Defense Council, Pennzoil Co., and Sierra Club by Clement Associates, November 11, 1982.

Nisbet, I.C.T., Rodricks, J.V., Wrenn, G.C., Dippel, C., Helms, G.L., Karch, N.J., and Yost, L.J. 1982. Standard-setting: scientific and policy issues. A paper (including case studies) for the Cooperative Power Association by Clement Associates, January 19, 1982.

Karch, N.J. and Schneiderman, M.A. 1981. Explaining the urban factor in lung cancer, a report to the Natural Resources Defense Council; presented in testimony before the Subcommittee on Health and Environment, House Committee on Science and Technology, December 15, 1981.

Karch, N.J. 1980. Assessment of human health risks from ingestion of fish, seafood, and drinking water contaminated with crude oil. Testimony before the Washington Energy Facility Site Evaluation Council, Olympia, Washington, on behalf of the Northern Tier Pipeline Co.

Nisbet, I.C.T., Karch, N.J., and Schneiderman, M.A. 1980. Comments on a draft paper by Doll and Peto on cancer numbers, Office of Technology Assessment, U.S. Congress, Contract No. 033-4810.0.

Karch, N.J. 1978. Polychlorinated biphenyls in the environment. In: The National Research Council in 1978. National Academy of Sciences, Washington, D.C. Pp. 220-224.

Karch, N.J. 1977. Explicit criteria and principles for identifying carcinogens: A focus of controversy at the Environmental Protection Agency. Vol. IIa: Case Studies. National Academy of Sciences, Washington, D.C. Pp. 119-206.

Karch, N.J., Koh, E.T., Whitsel, B.L., and McBride, J.M. 1975. An X-ray and EPR structural investigation of oxygen discrimination during the collapse of radical pairs in crystalline acetyl benzoyl peroxide. J. Am. Chem. Soc. 97:6729.

Karch, N.J., and McBride, J.M. 1972. Lattice control of free radicals from the photolysis of acetyl benzoyl peroxide. J. Am. Chem. Soc. 94:5092.

Karch, N.J. 1973. Two cases of solvent effects on photolytic decomposition. Ph.D. dissertation, Yale University.

Dr. Karch made significant contributions to the following:

Toxic Substances Strategy Committee. 1980. Report to the President. Toxic Chemicals and Public Protection. Author of: Chap. I: Environmental and public health problems; Chap. IV: Research activities in support of regulation; Chap. VII: Cancers and carcinogens: Preventive policy. U.S. Government Printing Office, Washington, D.C.

Council on Environmental Quality. 1980. Environmental quality, 1979. Tenth Annual Report of the President's Council on Environmental Quality. Chap 3: Toxic substances and environmental health. U.S. Government Printing Office, Washington, D.C.

Council on Environmental Quality. 1979. Environmental quality, 1978. Ninth Annual Report of the President's Council on Environmental Quality. Chap 4: Toxic substances and environmental health. U.S. Government Printing Office, Washington, D.C.

Interagency Regulatory Liaison Group (IRLG). 1979. Identification of potential carcinogens and estimation of risks. J. Nat. Can. Inst. 3:241-268.

Committee on Environmental Decision Making. 1977. Analytical Studies of the U.S. Environmental Protection Agency. Vol. II: Decision Making at the U.S. Environmental Protection Agency. National Academy of Sciences, Washington, D.C.

American Chemical Society. 1974,1975. Official Public Policy Statements of the American Chemical Society. Vol. I, Supplement to Vol. I, and Vol. II. Washington, D.C.

Dr. Karch has given the following speeches, seminars, and testimony:

Structure activity analyses under the Toxic Substances Control Act. Testimony before the Subcommittee on Commerce, Transportation, and Tourism of the House Committee on Energy and Commerce, April 21, 1983.

Dose-response relationships and extrapolation models. A seminar at the Walter Reed Army Research Institute, Preventive Medicine Program, October 18, 1982.

Risk assessment and environmental policy making: Current issues and future prospects. A seminar sponsored by the George Washington University Graduate Program in Science, Technology and Public Policy and the U.S. Environmental Protection Agency, July 21, 1982.

Proposed amendments to the pesticide law -- Confidentiality and its impact on risk assessment. Testimony before the Senate Committee on Agriculture, June 22, 1982.

Black/white differences in lung cancer rates: A clue to the role of environmental factors. Ninth Annual Research Colloquium, School of Human Ecology, Howard University, May 7, 1982.

Centralization of risk assessment and the separation of scientific evaluation from policy making: Issues and prospects. A speech before the Committee on Institutional Means for Risk Assessment, National Academy of Sciences, February 10, 1982.

Explaining the urban factor in lung cancer. Testimony before the Subcommittee on Health and Environment, House Committee on Science and Technology, December 15, 1981.

Procedures and evaluation criteria in the assessment of hazard, exposure, and risk. A faculty seminar before the Institute of Environmental Medicine, New York University, April 17, 1981.

Risk assessment procedures and policies: A critique of "Choosing our pleasures and our poisons: Risk assessment in the 1980s" by William W. Lowrance. A presentation at the Second NSF/AAAS Workshop on the Five Year Outlook for Science and Technology, December 11, 1980.

Federal regulation of chemical carcinogens. A faculty seminar in comparative risk. Massachusetts Institute of Technology, March 7, 1980.

Overview on the estimation of the role of environment in disease. A presentation to the Committee on the Costs of Environmentally-Related Diseases, Institute of Medicine, National Academy of Sciences, January 21, 1980.

Recent findings of the Toxic Substances Strategy Committee· Attributing environmental cancers to their causes. A presentation at the Third Annual Food Safety Council Public Policy Seminar, December 14, 1979.

The Toxic Substances Strategy Committee and the cancer policies of EPA, FDA, OSHA, and CPSC. A speech at the American Enterprise Institute Symposium on the Regulation of Occupational and Environmental Cancer, December 5, 1978.

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Dr. Golden has extensive experience in the evaluation of various environmental health hazards. Since 1975, Dr. Golden has directed several committees at the National Academy of Sciences. As part of these activities, he identified and evaluated the pertinent research literature on such subjects as toxicology, epidemiology, risk assessment, and water treatment technology. Under a Congressional mandate, a series of reports were prepared for the U.S. Environmental Protection Agency on drinking water and health. In addition, Dr. Golden worked with committees that investigated the potential carcinogenicity of pesticide products and the toxicology of various industrial chemicals.

During his tenure at the National Academy of Sciences, Dr. Golden was responsible for comprehensive evaluations of the adverse health effects that may result from the presence in drinking water of inorganic, organic, microbiological, radiological, and particulate contaminants. Furthermore, he helped to estimate the cancer risks from selected organic drinking water contaminants, the first such compilation of risk estimates from chemical contaminants in the environment. These estimates and other evaluations were published by the National Academy Press in a five volume series, Drinking Water and Health, which has gained wide acceptance in the scientific community.

Dr. Golden also worked on the resolution of a controversy involving the evaluation of the carcinogenicity of the pesticide ingredients, chlordane and heptachlor. The report was prepared at the request of an Administrative Law Judge of the U.S. Environmental Protection Agency. In resolving the scientific questions concerning the carcinogenicity of these pesticide chemicals, the committee established for the first time objective criteria for identifying cancerous lesions in the livers of mice. Dr. Golden also directed a comprehensive evaluation of the biological and environmental effects of selected aromatic and aliphatic amines for another committee. This included detailed assessments of acute and chronic toxicity, metabolism, and epidemiology.

Another subject for which Dr. Golden was responsible concerned the establishment of quality criteria by which treated wastewater may be judged acceptable for potable reuse. This required the development of an hierarchical series of predictive tests in which concentrated water samples are tested for potential toxicity.

EDUCATION

Ph.D., Environmental Toxicology, University of Michigan, 1975

M.S., Physiology and Pharmacology, Wayne State University, 1966

B.A., Biology, University of Michigan, 1964

EMPLOYMENT HISTORY

1983-present	Senior Associate, Karch & Associates
1979-1983	Project Director, National Academy of Sciences/ National Research Council
1977-1979	Assistant Project Director, National Academy of Sciences/National Research Council
1975-1977	Staff Officer, National Academy of Sciences/ National Research Council
1970-1975	Environmental Health Sciences Trainee, School of Public Health, University of Michigan
1969-1970	Lecturer in Biology, University of Michigan
1967-1969	Teacher, East Detroit High School
1966	Analytical Chemist, Sherman Drug Company

MEMBERSHIP IN SOCIETIES

Society of Toxicology

PROFESSIONAL EXPERIENCE

Project Director of the Safe Drinking Water Committee at the National Academy of Sciences; directed the completion of volumes 4 and 5 of Drinking Water and Health, which cover evaluations of selected organic and inorganic drinking water contaminants, and a review of the contribution of the distribution system to drinking water quality.

Assistant Project Director for the Safe Drinking Water Committee at the National Academy of Sciences; assisted in the preparation of volumes 2 and 3 of Drinking Water and Health, which evaluated selected drinking water contaminants, the problems of risk estimation, the contribution of drinking water to mineral nutrition, and a review of drinking water disinfection including the use of granular activated carbon.

Staff Officer for the Safe Drinking Water Committee at the National Academy of Sciences; assisted in the preparation of volume 1 of Drinking Water and Health, which reviewed the health effects of organic, inorganic, microbiological, particulate, and radiological contaminants of drinking water. Also developed were risk assessments for known or suspected carcinogens.
Project Director of the Committee on Amines at the National Academy of Sciences; directed a comprehensive review of the biological and environmental effects of selected aromatic and aliphatic amines.

Project Director of the Panel on Quality Criteria for Water Reuse at the National Academy of Sciences; this panel developed the scientific criteria by which treated wastewater may be tested to judge its acceptability for potable reuse.

PUBLICATIONS

Dr. Golden has made significant contributions to the following:

Drinking Water and Health, Volume 5. 1983. Safe Drinking Water Committee, Board on Toxicology and Environmental Health Hazards, National Reaserch Council, National Academy of Sciences, Washington, D.C., 280pp.

Drinking Water and Health, Volume 4, 1982. Safe Drinking Water Committee, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy of Sciences, Washington, D.C., 299pp.

Drinking Water and Health, Volume 3, 1980. Safe Drinking Water Committee, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy of Sciences, Washington, D.C., 413pp.

Drinking Water and Health, Volume 2, 1980. Safe Drinking Water Committee, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy of Sciences, Washington, D.C., 393pp.

Drinking Water and Health. 1977. Safe Drinking Water Committee. Advisory Center on Toxicology, National Research Council, National Academy of Sciences, Washington, D.C., 933pp.

Quality Criteria for Water Reuse. 1982. Panel of Quality Criteria for Water Reuse, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy of Sciences, Washington, D.C.,145pp.

Aromatic Amines: An Assessment of the Biological and Environmental Effects. 1981. Committee on Amines, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy of Sciences, Washington, D.C.,319pp.

Selected Aliphatic Amines and Related Compounds: An Assessment of the Biological and Environmental Effects. 1981. Committee on Amines, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy of Sciences, Washington, D.C., 168pp.

An Evaluation of the Carcinogenicity of Chlordane and Heptachlor. 1977. Pesticide Information Review and Evaluation Committee, Advisory Center on Toxicology, National Research Council, National Academy of Sciences, Washington, D.C., 120pp.

ABSTRACTS

Federation of American Societies for Experimental Biology, "Effects of Vitamin B12 Transformation Products on Absorption of Vitamin B12", Abstract #1351, April, 1966, Atlantic City, NJ.

Society of Toxicology, "Some Effects of Cadium Induced Hypertension on Vascular Smooth Muscle", Abstract #167, March, 1974, Williamsburg, VA.

First International Congress on Toxicology, "Health Effects of Drinking Water Contaminants", April, 1977, Toronto, Canada.

INVITED TALKS, SYMPOSIA AND PANELS

University of Texas at Austin, Lyndon B. Johnson School of Public Affairs, "Coping with the Safe Drinking Water Act - Nitrate and Fluoride Standards", April, 1978, Austin, TX.

University of North Carolina, School of Public Health, "Health Effects: Toxicological Considerations from Drinking Water Contaminants", May, 1978, Chapel Hill, NC.

University of West Virginia, "Toxicology and Risk Assessment from Chronic Exposure to Low Levels of Chemical Contaminants", March, 1978, Morgantown, WV.

University of West Virginia, "Chemical Carcinogens and Risk", March, 1979, Morgantown, WV.

University of Michigan, School of Public Health, "From the Lab Bench to the Law Bench: Science Becomes Policy", December, 1979, Ann Arbor, MI.

Americal Chemical Society, Division of Environmental Chemistry, "Safe Drinking Water; The Impact of Chemicals on a Limited Resource", August, 1983.

American Water Works Research Foundation, Workshop On Revised Primary Drinking Water Regulations, "Health Effects of Inorganic and Organic Chemicals", October, 1983, St. Louis, MO.

INVITED MEETINGS

Gordon Research Conference, Toxicology and Safety Evaluation, 1977.

Gordon Research Conference, Toxicology and Safety Evaluation, 1978.

Cold Spring Harbor Laboratory, Origins of Human Cancer, 1976.

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Ms. Wasserman has experience in the evaluation of various environmental health hazards. Since 1980, Ms. Wasserman has contracted with several Research and Development firms. Her responsibilities included researching and writing a monograph on the toxicology of ethylene oxide for the American Association of Railroads through the BDM Corporation. This monograph is incorporated into a report on the toxicology of chemicals transported by rail.

In addition to the above, Ms. Wasserman has also worked on toxicity validation studies at the U.S. Environmental Protection Agency (EPA), Washington, D.C.. These activities included writing the questions that would determine the type and degree of toxicity that a particular chemical exerted according to the reports on file.

Ms. Wasserman has done some pharmacological consulting with a law firm on an adverse drug reaction case. The possible side effects of a drug were researched and incorporated into a report to be used in a malpractice case.

EDUCATION

M.S., Pharmacology, The George Washington University, 1984

A.B., Biology & Economics, Washington University, 1980

EMPLOYMENT HISTORY

1983-present	Staff Scientist, Karch & Associates
1980-1983	Teaching Fellow, The George Washington University
1983	Consultant, Lucas & Asssociates ,P.C.
1982-1983	Consultant, Life Systems Inc.
1981	Consultant, BDM Corporation

Professional Society Memberships

American Society of Pharmacology and Experimental Therapeutics (student member)
New York Academy of Sciences (student member)
Association for Women in Science
Phi Delta Gamma Fraternity for Women Scholars

AWARDS AND HONORS

1982 Goddard Prize-Outstanding scholastic achievement in Pharmacology

being turned

REVIEW OF THE WOBURN HEALTH STUDY

By Department of Biostatistics

Harvard School of Public Health

Boston, MASS

This study was a joint, cooperative venture between the citizens group in Woburn (FACE) and the Harvard School of Public Health. A survey questionnaire was designed by the School's department of Biostatistics together with FACE. A total of 301 interviewers, primarily from Woburn, who were trained by the school administered the health questionnaires. Each interviewer was given 25 telephone numbers to call. These telephone numbers were from different areas of Woburn but it was not entirely clear to me how the 25 numbers for each interviewer were selected. Starting out with a total number of 10,310 telephone numbers, there was a 15 to 21% refusal rate. A total of 3,257 evaluable households were finally available. Loss of households was due to recent arrivals, no household member born after 1920, refusal rate and disconnected phones, business phones, second residence phones. All of this is outlined in Table 4.1 of the report. It is not stated in the document what the total population of Woburn is and what the total number of housholds is. Figure 4.3 gives a refusal rate by regions and there does not seem to be much difference in the different regions, however, it is not quite clear how these regions were developed and how those regions relate to the areas with presumed high and low water consumption from wells G and H.

It was estimated by the investigators that the amount of water consumed from wells G and H was different in different parts of town. This was determined

through a report which had been prepared by DEQE (Department of Environmental Quality Engineers). The report is entitled "Water Distribution System of Woburn, Massachusetts 1964-1979." The Department of Environmental Quality Engineers basis for estimating the contribution of wells G and H to the system relied on a simulation of a detailed model of the Woburn water system. The model was formulated using the metropolitan District Commissions Metropolitan Water Transmission and Distribution System simulating model. It appears that this was basically a mathematical model which was not verified by experimental data and is therefore open to question. It is for instance not clear whether the power of the motors used for water usage which would have resulted in changes in pressure in the water distribution system. It is also not clear whether it was considered that these wells were apparently only used intermittently. According to a CDC report (EPI 80-37-2 Sept. 16, 1981, see attached), well G began to pump in 1964 and was on-line until 1967 and from then to May 1979, was on and off depending on Woburn's water needs. Well H which started pumping in July 1967, was shut down from December 1967 until August 1974 and then used intermittently as needed. Then in May 1979, wells G and H were permanently shut down when organic contaminants were discovered. These organic contaminants listed in Table 8 of the CDC report are all in the parts per billion (micrograms per liter) range and are no higher than what has been found in many other areas in the United States. None of these solvents have been associated with the induction of leukemia or cancer of the kidney in humans. (Two types of tumors found in excess in Woburn by CDC investigators.) It is also not clear what is meant by intermittent use. Does this mean intermittent on a day-to-day basis or were the wells shut off several months at a time? For instance, if that were the case, this could greatly influence the exposure during pregnancy, particularly if these

pregnancies occurred partly during periods when the wells were actually shut off. No information is given about the other wells nor is any information given about any possible pollutants in the other wells.

Following the discussion of the water supply system in the Harvard study is a discussion of possible general exposure to ground water contaminated areas. However, no specific chemicals that would either cause leukemia or that have in the past been associated with other health problems where identified nor was it made clear how this general exposure to ground water contaminated areas would take place. For instance, even though toluene and benzene were detected in test wells in these contaminated area, this does not necessarily mean that people would come in contact with these materials.

If the data on the leukemia cases are reviewed, it appears that between 1969 and 1979, 12 leukemia cases were identified and according to the National average, only 5.3 cases should have occurred. Apparently, according to the CDC report, most of these leukemia cases were in boys. Boys had an elevated rate while girls overall did not. However, the girls cases were all diagnosed when they were between ages 10 and 14, and this represented a significant elevation for that age group (p=0.008). Cases were occurring among boys in all age groups and also in the age group of less than 1 to 4 years. Thus, it the water contamination had anything to do with the development of leukemia, such exposures would, in some cases, have been relatively short. The Harvard report indicates that a higher rate of leukemia cases is continuing in the area. For the period of 1980 to 1983 an additional 4 cases of childhood leukemia were identified. However, the water supply was shut off in 1979.

Unfortunately, the ages of these children are not given and it is not clear, for instance, whether the one case which is in the age group of 0-4 was actually a case which developed after the wells had been shut down.

The cut-off date for childhood leukemia used by CDC was 15 years while that used by the Harvard group is 19 years which also adds some differences to the two studies. The sex of the additional 4 cases of leukemia in the Harvard study is also not given. Although it is pointed out that 2 of the leukemia cases which are used in the statistics were not included in making the calculations for the cumulative exposure since they were born after the wells were shut down. These cases still seem to be included in the other statistics. There are apparently 5 other cases that also had no exposure. If the cumulative exposure for case A and case C were removed from the data set, then the exposures to water from wells G and H between the control group and the cases would be approximately equal. In fact, the total would then be 7.62 for the cumulative exposure cases versus a total of 6.02 in the control group. However, it is not entirely clear to me how these numbers were developed. This would have to be carefully checked and recalculated. The authors themselves point out on page 32 that the excess leukemia cases cannot all be linked to the wells.

Time did not permit me to examine in detail all of the studies made on other health outcomes. However, it should be pointed out that the spontaneous abortions (miscarriages) were determined to be those in which the embryo or fetus is prematurely expelled in the first 6 months of pregnancy. This is somewhat different from commonly used practice. In the Boston Hospital for

Women, to the best of my knowledge, all fetuses whether born alive or dead are regarded as abortions if they are born before 20 completed weeks of gestation. All fetuses surviving in utero beyond 20 weeks gestation must be reported to the health department. It should be determined what the present practice is in Massachusetts. The World Health Organization (WHO) has recommended that the use of the word "abortion" be discontinued and that the term "fetal deaths" be applied to all fetuses dying in utero with classifications into 4 groups: 1) Less than 20 weeks; 2) 20 - 28 weeks; 3) over 28 weeks; 4) unknown age. I am pointing this out because if the results are compared to other statistics which have been collected differently, then it must be determined what the criteria were for those other collection systems. The definition for paranatal mortality rate is also not quite clear and is perhaps somwhat different than from what has usually been recommended. I am attaching a xerox copy of several pages out of "Potter and Craig Pathology of the Fetus and Infant," which goes into the definition of these different periods and unless these baselines are better established, it is not clear how any comparisons can be made.

The same is true for the collection of birth defects. It is really not clear whether these were birth defects that were noted during the neonatal period, the first year of life or later, and the low birth weight was also not defined very well in that it was stated as being the proportion of 7 day survivors who weight less than 6 pounds at birth. Low birth weight data are usually collected somewhat differently in that all live births are recorded at the time of birth.

As far as paranatal mortality is concerned, page 44 was missing from the report I had and this could therefore not be evaluated. According to the authors (see page 47 of the report), there were 22 eye/ear defects and of these, 5 or 6 can be statistically explained by the well water. Then it is further stated that in the Pine Street and Sweetwater areas, 1.2 and 0.4 eye/ear anomalies were expected but 3 and 2 occurred. These numbers are very small and it would have to be determined in more detail what these eye/ear anomalies are and whether they should be grouped together. The investigators also grouped other birth defects and classified them as environmental defects. They included in environmental defects, defects of the central nervous system (spina bifida, anencephaly, cleft, down syndrome, and other chromosomal mutations). In this fashion, they collected 29 environmental birth defects. Maternal age was the only factor significantly correlated with the risk of such a defect. After controlling for maternal age and for the time period, a statistically significant elevation of environmental defects within the Pine Street area and with increasing exposure to wells C and H was still present. However, there were only 5 cases in the Pine Street area and only 3.6 could be statistically explained as having had increased exposure to wells G and H. It is not clear for instance, when these birth defects were established, what they actually represented and whether such confounders as medication taken during pregnancy were evaluated.

Childhood Diseases and Disorders

The childhood diseases and disorders were also grouped into broad categories. This was based partly on the need to produce larger numbers of events for study. On page 72, an example is given. The "anemia other blood disorder"

category contained 58% of actual anemias. Several cases of thalassemia trait, RH factor and other blood problems at birth, hemophelia, lead poisoning and hepatitis. Eight cases of diabetes and 10 cases of thyroid problems were categorized as glandular disease. Nine cases of high blood pressure and 10 heart murmurs were classified as the most common heart disorders. Since many of the diseases that were grouped together have different etiologies, such grouping is not acceptable. It is also not clear how the numbers of the expected rates for instance, for lung disorders and other diseases, were developed.

A questionnaire was either administered to the male or female head of the household. It is known that outcomes of pregnancy are usually better remembered by the female and it is not clear whether the analyses of the results were adjusted for that. If for instance, in one particular area, more of the females gave the information for the health interview, this in some way, could have biased the study. The questions in the questionnaire are rather open-ended and although the authors of the report state that they adjusted for smoking in their analyses, (I think they should also have adjusted for alcohol consumption) there are no such questions listed on the questionnaire nor are any questions asked about occupation.

Because of time constriants, the appendix which starts after the questionnaire (page A-8) was not examined.

Impression

After reviewing the EPI report (EPI-80-37-2) and the Harvard study, I am not impressed that the contamination of wells G and H with solvents had any effect on disease incidence in the Woburn area. There is an increase in childhood leukemia and in the CDC study, an increase in cancer of the kidney in adult males was also noted by the CDC investigators. It is highly likely that the increase in kidney cancer is related to occupation. In the 1980 CDC report, a number of recommendations were made. I think these recommendations should still be followed.

It is known that there were a number of tanneries in the Woburn area. These are associated with certain cancer risks in the occupationally exposed. I am attaching a copy of a paper by Decoufle (1979) outlining processes used in tanneries. A better assissment of occupational exposure in the Woburn area should be made. It should be determined what type of tanning processes were used and whether and what dyes were used. The potential carcinogens associated with the tanning industry are the hexavalent chromium products, arsenic, azo dyes and B napthylamine. In connection with the glue factory (also in Woburn) and with tanning, there are industrial processes which may result in nitrosamine waste materials.

I am also enclosing a copy of a paper on the mortality experience of arsenic exposed workers by Pinto et al. (1978), and finally, I am including a paper which discusses the possibility of a leukemia increase in children because of their exposure to high current flow and high intensity electro-magnetic fields (Wertheimer and Leeper 1979), and a letter to the editor stating that

electricians who are exposed to high intensity electro-magnetic fields, have more deaths than expected from acute-leukemia and lymphome. These various factors should be analyzed further.

It should be determined now extensive chemical contamination from the textile and paper industries as well as tne animal glue industry was and whether any residues remain from those activities as well as the tanneries. Furthermore, lead, as leadarsenate, was also used in the area. It should be determined whether any accesses of cancer in the adult population are due to occupational exposure and what the plausible routes of exposure for the children to carcinogens would be.

From the latest Woburn study I am not able to draw any conclusions as to whether any of the reported health problems are associated with living in Woburn.

Comments of Renate D. Kimbrough, M.D.

February 27, 1984

Deputy Chief, Cancer Branch, CDD, CEH

Review of the manuscript, "Synopsis: The Woburn Health Study, An Analysis of Reproductive and Childhood Disorders and their Relation to Environmental Contamination," by S. W. Lagakos, B. Wessan, and M. Zelen

Vernon N. Houk, M.D.
Director, Center for Environmental Health

Lee James, Melissa Adams, and Cynthia Berg from the Birth Defects Branch, CDD, and Nancy Hicks and I from the Cancer Branch, CDD, have reviewed this manuscript. Because it seems to have been written for a lay, rather than a scientific, audience, we prefer to give the authors the benefit of the doubt and not to render judgment on the current version. It lacks details of methodology that make it impossible to evaluate the validity of the report's conclusions. Once the final report becomes available, we would be willing to review it.

Some of the major problems in the current synopsis that the authors may remedy in the final report are

1. The possibility of selection bias because of the large percentage (46%) of nonrespondent households: parents of children with disorders living in the well publicized, suspect neighborhoods of Woburn may have been more willing to respond to such a survey than other groups.

2. The index of exposure used, perhaps the only available measure of exposure, estimates only the availability of water, not the actual use of water, in the household or by the individual.

3. The definitions of some of the outcomes and their confirmation by an independent source are lacking. Would, for example, the "lung and respiratory disorders" include common disorders like colds? When and at what ages did these disorders occur? If a disorder required medical treatment, does this indicate a more severe disorder or only increased parental concern?

4. How, specifically, the authors adjusted their analyses of reproductive disorders for "all relevant risk factors. . . . [using] multivariate models" (pp 10-11) remains unclear.

5. Are the observed associations likely to be causal?

Matthew Zack

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